ABSTRACTS

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ABSTRACTS

BELGIAN ASSOCIATION FOR THE STUDY OF THE LIVER (BASL) / BELGIAN LIVER INTESTINE COMMITTEE (BLIC)

- A01 –

TOLL-LIKE RECEPTOR 2 ACTIVATION IN MONOCYTES OF ALCOHOL USE DISORDER PATIENTS CONTRIBUTES TO SYSTEMIC INFLAMMATION AND ALCOHOL-ASSOCIATED LIVER DISEASE. L. Maccioni (1), J. Kasavuli (1), S. Leclercq (2), B. Pirlot (1), G. Laloux (3), Y. Horsmans (4), I. Leclercq (1), B. Schnabl (5), P. Stärkel (1) / [1] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, Laboratory of Hepato-gastroenterology, [2] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, Metabolism and Nutrition Research Group, Louvain Drug Research Institute, Institute of Neuroscience, [3] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, de Duve Institute, [4] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Department of Hepato-gastroenterology, [5] University of California San Diego, La Jolla, United States, Department of Medicine.

Introduction: A minority of alcohol use disorder (AUD) patients develops progressive alcohol-associated liver disease (ALD) potentially linked to gut barrier dysfunction, microbial translocation and activation of systemic immune responses. Activation of circulating monocytes by microbial products might contribute to systemic and liver inflammation leading to ALD progression. Human data linking monocytes to early stages of ALD are lacking.
Aim: We explored the links between changes in monocytes, microbial translocation, systemic inflammation and monocyte-derived macrophages in early human ALD.
Methods: We included n=123 AUD patients following a highly standardized rehabilitation program and n=26 healthy controls. We determined the total number of monocytes and proportion of monocytes subsets by FACS. Serum microbial translocation markers and cytokines were measured by ELISA and multiplex assay, respectively. Cytokines reflecting activation of monocytes were assessed by qPCR. Toll-like receptor (TLR) expression in monocytes and activation as well as phagocytosis were assessed in vitro. ALD severity and liver inflammatory responses were analyzed in liver biopsies by histology, qPCR, immunohistochemistry and ELISA.
Results: In AUD patients, the number of blood monocytes increased ($p<0.0001$). Among the 3 monocyte subpopulations, intermediate and non-classical increased while classical monocytes decreased compared to controls. Monocytes from AUD patients up-regulated IL1β and IL8 together with TLR2 and down-stream AP-1. IL1β and IL8 were actively secreted by those monocytes upon stimulation in vitro with the TLR2 ligand Peptidoglycan. Stimulation with E. coli confirmed preserved bacterial phagocytic activity. Systemic levels of cytokines and alterations in monocytes correlated with microbial translocation markers. In parallel, IL1β and IL8 were increased in ALD livers together with activation of intrahepatic macrophages (CD163+, iNOS+, TREM1+). Liver chemokines (MCP1, CX3CL1) involved in monocytes attraction were induced in liver tissue. IL1β and IL8 correlated with liver chemokines, iNOS+ up-regulation in macrophages and ALD severity markers (e.g. fibrosis, AST/ALT, CK18-M65 and M30).
Conclusions: Our results point to a contribution of activated monocytes to systemic and liver inflammation. Monocytes likely infiltrate the liver, transform into monocyte-derived macrophages and release IL1β and IL8 in response to Peptidoglycan and TLR2 activation, ultimately leading to ALD progression.

- A02 –

ACCURACY OF NON-INVASIVE TECHNIQUES COMPARED TO MAGNETIC RESONANCE SPECTROSCOPY TO EVALUATE THE PRESENCE OF FATTY LIVER DISEASE IN INDIVIDUALS WITH TYPE 1 DIABETES: INITIATE1 STUDY. J. Mertens (1), M. Spinhoven (2), E. Dirinck (3), L. Vonghia (1), C. De Block (3), S. Francque (1) / [1] University of Antwerp/Antwerp University Hospital, Edegem, Belgium, Gastroenterology and Hepatology, [2] University of Antwerp/Antwerp University Hospital, Edegem, Belgium, Radiology, [3] University of Antwerp/Antwerp University Hospital, Edegem, Belgium, Endocrinology, Diabetology and Metabolism.

Introduction: The global prevalence of nonalcoholic fatty liver disease (NAFLD) is rising due to its connection with overweight, metabolic syndrome, and type 2 diabetes. The epidemiology of NAFLD in individuals with type 1 diabetes (T1D) is uncertain, partly due to the lack of cross-validation of non-invasive techniques (NITs) to assess liver steatosis.
Aim: This study aimed to determine the accuracy of commonly used NITs in a T1D cohort in order to evaluate their usefulness in a clinical screening algorithm tailored to T1D.
Methods: Patients with T1D who consented underwent abdominal ultrasound scoring (USS), Fibroscan® to determine the controlled attenuation parameter (CAP), and magnetic resonance spectroscopy (MRS). The Fatty Liver Index (FLI) was also calculated based on waist circumference, body mass index, gamma-glutamyltransferase, and triglycerides. A mean liver fat content ≥ 6.0% on MRS our of three measurements was considered diagnostic (reference standard). Secondary causes of liver steatosis were ruled out in all.
Results: 119 adults with T1D were consecutively included. According to MRS, NAFLD was present in 17 cases (14%). NAFLD prevalence was 16% based on USS, 30% based on FLI ≥ 60, and 61% based on a CAP value ≥ 248 dB/m (on

machine-selected preferred probe). USS yielded an area under the receiver-operator curve (AUROC) of 0.93 (0.84-1.00). AUROC of the combined CAP (preferred probe) was 0.77 (0.67-0.88), while the M probe CAP (M-CAP) and XL probe CAP (XL-CAP) had AUROCs of 0.87 (0.79-0.95), and 0.69 (0.54-0.84) respectively. FLI yielded an AUROC of 0.62 (0.48-0.76). The optimal CAP cutoff was 270 dB/m, regardless of the probe. USS had a good sensitivity of 88%, with a specificity of 96%, while the conventional cutoff of FLI ≥ 60 only had a sensitivity of 38%, with a specificity of 72%. The CAP ≥ 270 dB/m (preferred probe) had a sensitivity of 93% with a specificity of 64%. Correlation was relatively strong between the two probes ($r = 0.68$, $p < 0.001$). To evaluate the agreement between the two probes, we constructed a Bland-Altman plot from 62 subjects that had results obtained from both probes. Linear regression of the differences between the probes compared to the mean ruled out proportional bias. When compared qualitatively, there is fair agreement ($k = 0.47$, $p < 0.001$) between the two probes. Combining USS with a CAP ≥ 270 dB/m yielded an AUROC of 0.89 (0.78-1.00), a sensitivity of 81%, and a specificity of 97%.
Conclusions: Ultrasound and CAP ≥ 270 dB/m are useful NITs to screen for NAFLD, with the potential of increased accuracy when combined in a screening algorithm, while FLI is highly unreliable in individuals with T1D and should not be included.

- A03 -

SINGLE-CELL ATLAS OF ADIPOSE TISSUE MACROPHAGES IN NON-ALCOHOLIC FATTY LIVER DISEASE. M. Boesch (1), H. Korf (1), R. Feie-Azevedo (1), A. Lindhorst (2), E. Deleus (3), M. Lannoo (3), L. Smets (1), L. Van Melkebeke (1), M. Wallays (1), T. Roskams (4), P. Bedossa (5), J. Verbeek (1), T. Voet (6), A. Sifrim (6), M. Gericke (2), S. Van Der Merwe (1) / [1] KUL - University of Leuven, Leuven, Belgium, Laboratory of Hepatology, CHROMETA Department, [2] Leipzig University, Leipzig, Germany, Institute of Anatomy, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Abdominal Surgery, [4] KUL - University of Leuven, Leuven, Belgium, Department of Imaging and Pathology, [5] Beaujon Hospital Paris Diderot University, Paris, France, Department of Pathology, Physiology and Imaging, [6] KUL - University of Leuven, Leuven, Belgium, Department of Human Genetics.

Introduction: Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease, thereby affecting 25% of the world population. Patients with non-alcoholic fatty liver (NAFL) can progress further to non-alcoholic steatohepatitis (NASH), characterized by steatosis and hepatic inflammation. It has been postulated that ongoing inflammation in the adipose tissue compartment, potentially driven by macrophages, accounts for this disease transition. Previous studies already showed a significant heterogeneity within the macrophage pool in obese adipose tissue.
Aim: We aim to unravel the human visceral adipose tissue macrophage population on a single cell level in a well-defined human NAFLD population.
Methods: Visceral adipose tissue (VAT) biopsies were collected from obese patients undergoing bariatric surgery (UZ Leuven, Belgium). Liver biopsies were performed and assessed by expert liver pathologists based on the fatty liver inhibition of progression (FLIP) algorithm and steatosis, activity, and fibrosis (SAF) score to distinct patient groups. Adipose tissue macrophages were freshly dissociated and single cell RNA-seq was performed using 10X Genomics 3′v3 on samples of 2 obese controls without NAFLD, 3 NAFL and 4 NASH patients.
Results: The VAT contains multiple macrophage and monocyte subtypes with distinct transcriptional profiles. Among these we observed an increased influx of pre-Inflammatory macrophages and pro-inflammatory monocytes in patients with NASH compared to their obese counterparts. Additionally, anti-inflammatory/angiogenic macrophages were almost completely absent in tissue from NASH patients as compared to obese controls. Velocity and pseudotime analysis also revealed that these macrophages are no longer replenished in NASH patients.
Conclusions: Our study characterized the landscape of human adipose tissue macrophages that points towards a NASH-related loss of anti-inflammatory/angiogenic macrophages. Further studies unraveling their tissue localization and function are ongoing.

- A04 -

SINGLE CENTER EXPERIENCE WITH INTESTINAL TRANSPLANTATION. M. Clarysse (1), A. Dubois (1), L. Ceulemans (2), E. Canovai (1), I. Jochmans (1), L. Wauters (3), M. Hiele (3), T. Vanuytsel (3), D. Monbaliu (1), J. Pirenne (1) / [1] University Hospitals Leuven, Belgium, Leuven Intestinal Failure and Transplantation Center (LIFT), University Hospitals Leuven, & Lab of Abdominal Transplantation, Department of Microbiology, Immunology and Transplantation, KU Leuven, Leuven, Belgium, [2] University Hospitals Leuven, Belgium, Leuven Intestinal Failure and Transplantation Center (LIFT), University Hospitals Leuven, & Lab of Respiratory Diseases and Thoracic Surgery (BREATHE), Department of Chronic Diseases and Metabolism, KU Leuven, Leuven, Belgium, [3] University Hospitals Leuven, Belgium, Leuven Intestinal Failure and Transplantation Center (LIFT), University Hospitals Leuven, & Lab of Translational Research in GastroIntestinal Disorders (TARGID), Department of Chronic Diseases and Metabolism, KU Leuven, Leuven, Belgium.

Introduction: Intestinal Transplantation (ITx) is a life-saving treatment for patients with complicated intestinal failure and patients with extensive portomesenteric thrombosis. Since October 2000, ITx has been performed in our center. We use strict donor selection criteria with young donors, who were not longer than 1 week admitted at the intensive care unit. Moreover, we have introduced the “Leuven immunomodulatory protocol” since the beginning, as preclinical studies revealed promising results. This protocol combines donor-specific blood transfusion, low immunosuppression levels and anti-inflammatory drugs to promote graft acceptance.
Aim: This single center retrospective study analyzes the long-term outcome with ITx.
Methods: All ITx recipients, transplanted at the University Hospitals Leuven, Belgium, between October 2000 and November 2021 were included in this retrospective cohort study. Data were prospectively collected and included donor cause of death, donor and recipient age and sex, transplant indication, acute and chronic rejection, graft and patient survival. Results are reported as median (interquartile range). Graft and patient survival rates were assessed by Kaplan-Meier analyses. Data were analyzed with GraphPad Prism 9.1.2 (GraphPad Software Inc., La Jolla, CA, USA).
Results: In total, 25 ITx (11 female, 4 pediatric transplants) have been performed with median recipient follow-up time of 6 (2-10) years. Median donor age was 16 (9-21) and all donated after brain death (DBD) (traumatic brain injury [n=16], intracranial bleeding [n=3], asphyxia [n=3], bacterial meningitis [n=1], and hydrocephaly [n=1]), except for one living donor. Median recipient age was 41 (25-48). Indications for ITx were life-threatening complications of intestinal failure due intestinal failure associated liver disease (IFALD) [n=6], recurrent catheter sepsis [n=5], quality of life [n=5], and lack of vascular access [n=1]. All of these were secondary to short bowel resulting from ischemia [n=9] or Crohn’s disease [n=2], chronic intestinal pseudo-obstruction [n=4], tumor [n=1], and microvillus inclusion disease [n=1]. Indications with extensive portomesenteric thrombosis were due to liver cirrhosis [n=4] and tumor [n=1]. In three patients, re-transplantation was performed after acute severe rejection necessitating urgent transplantectomy [n=2] or chronic rejection [n=1]. The majority were isolated bowel transplants [n=12], followed by combined liver-intestine transplantation [n=8], and multivisceral transplants [n=5]. In 7 cases, a kidney was simultaneously transplanted. Peroperative visceral artery embolization, dramatically reducing blood loss, was performed as of 2007 in all multivisceral cases and 1 re-transplant. The Leuven immunomodulatory protocol was used in 21 recipients. Acute cellular rejection occurred in 56% of recipients, which was severe (grade 3) in 28% [n=7]. Chronic rejection [n=2; 8%] was diagnosed 7 months and 14 years post-ITx. Acute, mild (grade 1), graft-versus-host disease was successfully treated in 1 recipient. Six grafts failed during follow up, caused by acute or chronic rejection [n=4, 16%], transmural ischemia [n=1], or refractory cytomegalovirus infection [n=1]. Seven recipients died, due to Aspergillosis-sepsis [n=2], NSAID-induced graft ischemia, sepsis, tumor recurrence, cardiac arrest, and multi-organ failure [one patient each]. At autopsy, a post-transplant lymphoproliferative disorder was diagnosed in 1 recipient. Of the 15 survivors, all are nutritionally independent. Graft survival rates were 79% at 1 year, 70% at 5 years, and 64% at 10 years. Patient survival rates at 1, 5, and 10 years were 88%, 76%, and 64%, respectively.
Conclusions: With strict donor selection criteria, in combination with the Leuven immunomodulatory protocol, long-term outcomes after ITx are comparable with those of other solid organ transplants.

- A05 -

DELETION OF HEPATIC GLUTAMINE SYNTHETASE PROMOTES NASH AND NASH-ASSOCIATED HCC. C. Pichon (1), M. Nachit (1), I. Leclercq (1) / [1] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, Institut de Recherche Expérimentale et Clinique - Laboratoire de Hépato-Gastro-Entérologie (GAEN).

Introduction: NAFLD represents a spectrum of diseases ranging from benign steatosis (NAFL) to nonalcoholic steatohepatitis (NASH). In cirrhosis and NASH, hepatic ammonia detoxification by urea cycle and glutamine synthetase (GS) is impaired, causing systemic hyperammonemia (excess of circulating ammonia). The impact of hyperammonemia on the evolution of liver disease is poorly known.
Aim: We want to evaluate the impact of glutamine synthetase loss of function in hepatocytes, on ammonia detoxification and on NAFLD evolution.
Methods: We injected to transgenic Glul floxed mice AAV8-TBG-Cre adenovirus to express the Cre recombinase and invalidate the GS gene (Glul) in >99% of hepatocytes (GS^{KO}) or saline to keep GS expression (GS^{WT}). GS^{KO} and GS^{WT} mice were then fed a high fat, high cholesterol diet (40% fat, 0,2% cholesterol) with 30% fructose in drinking water (Western diet + fructose: WDF) to induce NAFLD/NASH, or a standard rodent chow for control (C). We monthly recorded body weight, glycemia and circulating ammonia concentrations, and performed micro-computed tomography to monitor changes in liver fatty infiltration. At the end of the experiment (42 weeks), mice were sacrificed and the livers examined by histology.
Results: Blood ammonia concentration was similar in chow fed mice whether GS^{WT}-C or GS^{KO}-C. WDF feeding increased ammonia levels in GS^{KO} as from 12weeks and to the end of the study but not in GS^{WT} such as ammonia concentration was 95.4±22.8 µg/dl versus 72.8±10.6 µg/dl, in GS^{KO}-WDF and GS^{WT}-WDF at week 12, respectively, $p=0.0046$). Irrespective of the GS expression status, mice fed WDF consumed more calories and gained more weight than on a chow. While normal in chow-fed mice, glycemia was elevated in mice fed the WDF and was higher in GS^{KO}-WDF compared to GS^{WT}-WDF mice (255±32 mg/dl versus 181±19 md/d, respectively, $p<0.0001$). High glycemia in

GS^{KO}-WDF was associated with low insulinemia compared to GS^{WT}-WDF mice (3.97±2.07 µg/L versus 9.64±5.27 µg/L, respectively p=0.045). While liver density was stable around 0.95 H.U. over the study period in GS^{WT}-C as in GS^{KO}-C, consumption of the WDF was associated with a progressive and parallel lowering of liver density in both GS^{WT}-WDF and GS^{KO}-WDF signing steatosis. However, as from week 20 and to the end of the study, liver density was lower in GS^{KO}-WDF than in GS^{WT}-WDF mice (-0.108±0.184 H.U. versus 0.295±0.183 H.U. at week 20, respectively, p=0.0001). At sacrifice, the gross appearance of the liver was normal in GS^{WT}-C and GS^{KO}-C. In GS^{WT}-WDF the liver was enlarged and even larger with a striking nodular aspect in all GS^{KO}-WDF animals (3.47±0.96 g versus 5.40±0.97 g, respectively, p=0,0298). Liver histology (H&E staining) was mainly normal in chow fed GS^{WT} and GS^{KO}, it showed a zone 2 macrovesicular steatosis with mild inflammation, occasional ballooning and inconspicuous fibrosis in GS^{WT}-WDF. In GS^{KO}-WDF, there was a mixed micro/macrovacuolar panlobular steatosis with sustained periportal and lobular inflammation, ballooning and periportal and lobular F2 fibrosis. In addition, numerous well delimited nodules formed by proliferative atypical hepatocytes were seen in all GS^{KO}-WDF livers but not in any other group. GS IF staining confirmed the GS expression in one raw of central hepatocytes GS^{WT}-C, the increased GS expression to three raws of central hepatocytes in GS^{WT}-WDF and the absence of GS in all GS^{KO} (whether C or WDF) livers.
Conclusions: In mice fed a NASH-inducing WDF, deletion of hepatic glutamine synthetase causes hyperglycemia associated with insufficient insulin secretion. The deletion increased NASH severity and was associated with hepatocarcinogenesis. These results call for further exploration of the role of ammonia, glutamate and glutamine synthase pathways in NASH progression and as drivers of NASH-associated HCC.

- A06 -

DUCTULAR BILIRUBINOSTASIS IS INDEPENDENTLY ASSOCIATED WITH THE DEVELOPMENT OF ACLF AT SHORT TERM: RESULTS OF A PROSPECTIVE STUDY. L. Van Melkebeke (1), T. Ostyn (2), A. Broekhoven (3), H. Verspaget (3), S. Van Der Merwe (4), J. Verbeek (4), M. Coenraad (4), T. Roskams (2), F. Nevens (4) / [1] KUL - University of Leuven, Leuven, Belgium, Hepatology, [2] KUL - University of Leuven, Leuven, Belgium, Imaging and Pathology, Translational Cell and Tissue Research, [3] Leiden University Medical Center (LUMC), Leiden, The Netherlands, Gastroenterology and Hepatology, [4] KUL - University of Leuven, Leuven, Belgium, Gastroenterology and Hepatology.

Introduction: Alcoholic steatohepatitis (ASH) is one of the main precipitating events for the development of acute-on-chronic liver failure (ACLF). In 2010, ductular bilirubinostasis (DB) was identified as a marker of ACLF in alcoholic cirrhosis (Katoonizadeh A, Gut 2010).
Aim: Our aim was to validate this observation in a large prospective study with ASH patients, to investigate DB as a predictive marker for development of ACLF and to investigate the association of this finding with clinical parameters.
Methods: Prospective study in consecutive patients admitted with a diagnosis of ASH to a tertiary referral center between 03-2008 and 04-2021. Diagnosis of ASH was based on clinical presentation and confirmed by transjugular liver biopsy. All biopsies were assessed by a dedicated liver pathologist, who was blinded for clinical data and outcome, to score the grade of steatosis and grade of polymorphonuclear infiltration, and check for the presence of cirrhosis, parenchymal or ductular bilirubinostasis, ballooning and Mallory bodies. Clinical and histological data were collected from time of biopsy until 1 year follow-up. Diagnosis of ACLF was based on EASL-CLIF criteria. Differences between patients with and without ACLF at baseline were assessed using chi-square test. Predictors for development of ACLF within 28 days were assessed using univariate and multivariate Cox regression.
Results: 184 patients with biopsy-confirmed ASH were enrolled in the study with a median follow-up time of 365 days (IQR 83.5-365). At baseline, ACLF was present in 73 patients (39.7%). Another 30 patients developed ACLF within 28 days (median 7.5 days, IQR 2-20). At baseline, DB was the only histological parameter significantly more present in patients with ACLF compared to patients without ACLF (50.7% vs. 30.6%, p=0.007). When investigating predictors of development of ACLF within 28 days in a univariate analysis the following factors were significantly associated: Clinical data: infection (HR 2.10, 95%CI 1.41-3.05, p <0.001), creatinine (HR 1.72, 95%CI 1.49-1.99, p <0.001), bilirubin (HR 1.06, 95%CI 1.04-1.07, p<0.001), Maddrey-score (HR 1.01, 95%CI 1.01-1.02, p <0.001), MELD-score (HR 1.15, 95%CI 1.12-1.19, p<0.001), CLIF-AD score (HR 1.08, 95%CI 1.06-1.10, p<0.001). Histology data: moderate versus severe polymorphonuclear infiltration (HR 1.79, 95%CI 1.16-2.76, p=0.008) and DB (HR 1.61, 95%CI 1.09-2.38, p=0.02). In a multivariate model with infection, DB and grade of polymorphonuclear infiltration, all three were independently associated with the development of ACLF at 28 days (p<0.001, p=0.02 and p=0.008, respectively).
Conclusions: In this prospective study we confirm that DB is a histological marker for ACLF in patients with ASH. Furthermore, in this patient group with active alcohol intake, we show that DB is associated with short term development of ACLF, independently from the presence of infection. Our findings highlight that patients with ASH without ACLF but with ductular bilirubinostasis on liver biopsy should be followed up closely.

- A07 -

MONOCYTE SIGNATURES OF RECOVERY- AND NON-RECOVERY ACLF PATIENTS – UNCOVERING FUNCTIONAL, TRANSCRIPTOMIC AND METABOLIC DYNAMICS. R. Furtado Feio De Azevedo (1), H. Korf (1), M. Boesch (1), S. Radenkovic (2), M. Wallays (1), L. Smets (1), L. Van Melkebeke (1), B. Ghesquière (2), D. Cassiman (3), P. Meersseman (4), H. Van Malenstein (3), F. Nevens (3), W. Laleman (3), J. Verbeek (3), S. Van Der Merwe (3) / [1] KUL - University of Leuven, Leuven, Belgium, CHROMETA - Lab Hepatology, [2] VIB Center for Cancer Biology, Leuven, Belgium, Metabolomics Expertise Center, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department Gastroenterology and Hepatology, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Internal Medicine.

Introduction: Cirrhosis is the end-result of a progressive chronic liver disease that is largely asymptomatic, but if the insult persists, it may progress to the development of ascites, variceal haemorrhage and encephalopathy. A precipitating event can trigger deterioration of liver function and organ failure: termed acute-on-chronic liver failure (ACLF). ACLF is a devastating clinical entity with a mortality rate of up to 70% within a 28-day period. It is still not known if patients have infections due to a failure of monocytes in dampening the production of pro-inflammatory mediators, or whether a prolonged anti-inflammatory response make these patients incapable to respond to a secondary infection. Likewise, the functional and metabolic defects in ACLF are incompletely understood, which may be the key to restoring immune dysfunction.
Aim: We aim to study the dynamics of monocyte function during the course of ACLF progression and how it associates with the disease outcome.
Methods: We performed paired transcriptional, functional and metabolic analysis of CD14+CD16- isolated monocytes at day 0 and 7 from recently diagnosed ACLF patients to compare profiles in recovery vs non-recovery. ACLF patients with a CLIF-SOFA of 2/3 with underlying chronic alcoholic liver disease and no corticoid therapy were included in the study and were followed for 28 days after admission.
Results: Transcriptomic analysis unraveled a distinct pattern between ACLF non-recovery and recovery patients at baseline together with expression differences between day 0 and 7 in each group. Monocytes of non-recovery ACLF showed an impaired phagocytic capacity, oxidative response and incapability of inducing CD4+T cell proliferation as well as low capacity to trigger Tcell activation. Conversely, ACLF patients that recovered showed an improvement in phagocytic and oxidative burst capacity from day 0 to 7 and despite being inefficient in triggering Tcell proliferation, they featured an intact ability to induce Tcell activation. In addition, monocyte metabolic profile of recovery patients clustered separately from non-recovery ACLF patients at day 0. Additionally, the monocyte metabolic profile of the two groups clustered separately at day 0 and 7.
Conclusions: These findings provide necessary insight into the pathomechanism of recovery vs non-recovery ACLF. The immune phenotype seen in monocytes from recovery-ACLF patients points to the response to an infectious challenge. Notably, monocytes from non-recovery ACLF patients show functional impairment, which explains a poor immune response against infections.

- A08 -

A HISTORY OF BARIATRIC SURGERY IS INDEPENDENTLY ASSOCIATED WITH A YOUNGER AGE OF SEVERE ALCOHOLIC HEPATITIS ONSET, BUT IS NOT ASSOCIATED WITH SHORT-TERM SURVIVAL. L. Van Melkebeke (1), T. Ostyn (2), A. Broekhoven (3), M. Coenraad (4), H. Korf (1), T. Roskams (2), S. Van Der Merwe (1), F. Nevens (1), J. Verbeek (5) / [1] KUL - University of Leuven, Leuven, Belgium, Hepatology, [2] KUL - University of Leuven, Leuven, Belgium, Imaging and Pathology, Translational Cell and Tissue Research, [3] Leiden University Medical Center (LUMC), Leiden, The Netherlands, Gastroenterology and hepatology, [4] Leiden University Medical Center (LUMC), Leiden, The Netherlands, Gastroenterology and Hepatology, [5] KUL - University of Leuven, Leuven, Belgium, hepatology.

Introduction: Patients with prior bariatric surgery (BS) are at risk to develop an alcohol use disorder (AUD).
Aim: We assessed the effect of prior BS on disease profile and outcome of patients with severe alcoholic hepatitis (sAH).
Methods: From 01/2008 to 04/2021, consecutive patients admitted to our tertiary referral center with biopsy-proven sAH were included in a prospective database. Corticosteroid response was defined as a Lille score <0.45. Student's t-test, Wilcoxon rank sum test and Fisher's exact test were used according to the type of data. A cox proportional hazards model was used to compare survival. A p-value < 0.05 after multiple testing correction was considered significant.
Results: We identified 158 sAH patients with a median follow-up of 366 (68-1656) days. 28 (18%) patients had a history of BS (BS-group): 27 (96%) underwent bypass surgery and 1 patient gastric banding. No patient underwent sleeve gastrectomy. The proportion of patients with BS increased significantly over time: 4 (8%) within the first 5 years, 11 (19%) within the following 5 years and 13 (28%) during the last 4 years of the study period (p = 0.02). Patients in the BS-group were significantly younger at diagnosis of sAH (44.3 ±8.1 vs 52.4 ±10.3, p <0.001), were more frequently female (20 (70%) vs 50 (38%), p=0.02), had a higher body mass index (BMI) (29.7 ± 4.9 vs 26.6 ± 5.0, p=0.02) and a higher grade of steatosis on liver biopsy (p=0.03), compared to the non-BS-group. There were no differences in disease severity, measured by Maddrey-score (56.3 (37.8-75.2) vs 53.6 (40.6-70.9), p=0.71), MELD-score (23.3 (20.7-29.9) vs 24.0 (21.1-27.6), p=0.97) or histological parameters (polymorphonuclear infiltration (p=0.53), Mallory bodies (p=1), ballooning (p=0.47)) between the BS and non-BS group respectively. The correlation between BS and a younger age

at diagnosis remained significant after correction for sex, steatosis and BMI in a multivariate regression analysis ($p < 0.001$). There were no differences in corticosteroid response (14 (74%) vs 56 (66%), p=0.60), 28-day survival (27 (96%) vs 118 (91%), p=0.47), 90-day survival (24 (86%) vs 90 (70%), p=0.10) or overall survival (p=0.40) between the two groups.

Conclusions: In this prospective study, we showed that the proportion of sAH patients with prior BS has increased 3-fold over the last 15 years. Bypass surgery is independently associated with younger age of sAH onset, but not with corticosteroid response or short-term survival. Interestingly, all patients but one in the BS-group underwent bypass surgery, compared to other types of bariatric surgery. These novel findings indicate the need for early and effective prevention of AUD and sAH in patients who underwent bypass surgery.

- A09 -

UTILITY AND PROGNOSTIC VALUE OF DIAGNOSING METABOLIC DYSFUNCTION-ASSOCIATED FATTY LIVER DISEASE (MAFLD) IN PATIENTS UNDERGOING LIVER TRANSPLANTATION FOR ALCOHOL-RELATED LIVER DISEASE. B. Vanlerberghe (1), H. Van Malenstein (2), M. Sainz-Barriga (3), D. Monbaliu (3), S. Van Der Merwe (2), J. Pirenne (3), F. Nevens (2), J. Verbeek (2) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] University Hospitals Leuven, Belgium, Department of Gastroenterology and Hepatology, [3] University Hospitals Leuven, Belgium, Abdominal Transplantation Surgery.

Introduction: The term metabolic dysfunction-associated fatty liver disease (MAFLD) has recently been proposed to replace non-alcoholic fatty liver disease (NAFLD) as the overarching concept to define liver disease associated with systemic metabolic dysfunction. The new nomenclature and accompanying diagnostic criteria allow the identification of patients with metabolic dysfunction leading to liver disease in the presence of (prior) excessive alcohol use and consequently in patients with alcohol-related liver disease (ALD). The utility and prognostic value of MAFLD at the moment of liver transplantation (LTx) in patients with ALD has not yet been studied.

Aim: We assessed the prevalence of MAFLD in ALD patients undergoing LTx and its prognostic value on perioperative mortality, overall survival, recurrent hepatic steatosis and cardiovascular (CV) morbidity.

Methods: We retrospectively analyzed all patients transplanted for ALD between 1990 and August 2020 at our center. MAFLD at LTx was diagnosed based on the presence or history of hepatic steatosis and a BMI ≥25 kg/m2 or type II diabetes (DMII) or ≥2 metabolic risk abnormalities (dyslipidemia, hypertension, pre-diabetes). Overall survival and potential risk factors for recurrent liver steatosis (based on imaging or biopsy) and CV morbidity (CV events, atrial fibrillation and heart failure) were analyzed by Cox regression (presented as hazard ratio (HR) with 95% confidence interval).

Results: Of the 371 included ALD patients, 255 (68.7%) had concomitant MAFLD at LTx. 76.9% of ALD-MAFLD patients had a BMI ≥25 kg/m2 and 41.6% of ALD-MAFLD patients had DMII. Median follow-up post-LTx was 72 months (interquartile range (IQR: 34.5-122.0) and did not differ between ALD-MAFLD and ALD-non-MAFLD patients (median: 68.0 (IQR: 33.5-116.5) vs. 82.0 months (IQR: 35.5-127.5); p = .337). Patients with ALD-MAFLD were older (median: 61.0 (IQR: 56.0-76.0) vs. 58.0 years (IQR: 52.5-64.0); p = .001), more often male (86.3% vs. 66.4%, p < .001), and more frequently had hepatocellular carcinoma (HCC) at LTx (44.3% vs. 25.0%, p < .001). Perioperative mortality (2.75% vs. 1.72%, p = .553) and overall survival (HR: 0.991 (0.702-1.401); p = .960) did not differ between ALD-MAFLD and ALD-non-MAFLD patients. Multivariate analysis identified MAFLD at LTx (HR: 2.092 (1.412-3.098)), weight gain in the 1st year post-LTx (HR: 1.092 (1.043-1.143)) and any alcohol relapse (HR: 4.606 (3.097-6.850)) as independent risk factors for recurrent hepatic steatosis (p < .001). MAFLD at LTx was not associated with CV events (HR: 1.519 (0.790-2.922); p = .210), de novo atrial fibrillation (HR: 1.608 (0.864-2.992); p = .134) or de novo heart failure (HR: 1.091 (0.534-2.229); p = .811) post-LTx. This in contrast with traditional risk factors at LTx: age (HR: 1.064 (1.016-1.114); p = .008) and DMII (HR: 2.068 (1.134-3.770); p = .018) for CV events; BMI (HR: 1.072 (1.017-1.131); p = .010), age (HR: 1.042 (1.001-1.086); p = .047) and a history of a CV event pre-LTx (HR: 2.155 (1.010 – 4.597); p = .047) for de novo atrial fibrillation and a history of a CV event pre-LTx (HR: 3.590 (1.289-9.999); p = .014) for de novo heart failure.

Conclusions: The presence of MAFLD in ALD is associated with a distinct patient profile at LTx and is a risk factor for recurrent hepatic steatosis irrespective of alcohol relapse, but not for cardiovascular morbidity and overall survival. These novel findings demonstrate the utility and prognostic value of diagnosing MAFLD at LTx.

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PREVALENCE, PROGNOSIS AND FEATURES OF INCIDENTALLY DETECTED HEPATOCELLULAR CARCINOMA IN EXPLANTED LIVERS. E. Kerstens (1), S. Iesari (2), G. Dahlqvist (1), E. Bonaccorsi (3), L. Coubeau (3), O. Ciccarelli (3), B. Delire (1) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Hepatogastroenterology, [2] Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Italy, General surgery and kidney trasplantation, [3] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, General surgery and abdominal transplantation.

Introduction: Liver transplantation (LT), originally applied as treatment for decompensated cirrhosis, currently represents the treatment of choice for hepatocellular carcinoma (HCC) in cirrhotic liver. As the availability of the graft are limited, the waiting period is often long and the cirrhotic patients run an increased risk of developing an HCC. After LT, the recurrence of the illness on the graft and the premature decease represents a failure of the treatment. Sometimes, an incidentally found hepatocellular carcinoma (iHCC) is diagnosed postoperatively after the analysis of the liver explant from patients who underwent LT for non-oncological indication. Data about the prevalence and prognosis of iHCC are scarce. This phenomenon deserves particular attention as it could affect the prognosis of liver graft recipients.

Aim: The aim of this study is to evaluate the prevalence of iHCC in our LT patients and to compare the mortality, the risk of recurrence and the clinical, biological, and histological features between patients who underwent LT for preoperatively known HCC (pkHCC) and patients with a postoperative diagnosis of iHCC.

Methods: We retrospectively reviewed 268 adult patients who underwent a LT at the Cliniques Universitaires Saint-Luc, Brussels, Belgium, from January 2010 to January 2020. Results were compared using Fisher's exact test or Mann-Whitney U test as appropriate. The Kaplan-Meier method was used to analyze the rate of death and graft loss. Log-rank tests were run to compare the survival curves. The significance of statistical tests was taken at a P value of < 0.05. Analyses were run with SPSS Statistics.

Results: Among the 268 adult patients who underwent LT, 98 cirrhotic patients were transplanted for a pkHCC while the prevalence rate of iHCC in decompemsated cirrhosis patients was 12 % (9/75). The remaining patients were transplantated for other indications. The iHCC patients tended to be younger than pkHCC patients. Alcoholic cirrhosis was predominant in the iHCC cohort (88.9 % versus (vs) 48 %, p = 0.032). As expected, the patients of the iHCC cohort had a higher MELD score at the time of registration on the waiting list (19.0 (17.0-20.0) vs 10.0 (8.0 - 13.0); p < 0.001) and at LT (19.0 (18.0 – 20.0) vs 10.0 (8.0 – 14.0); p < 0.001). Value of Child-Pugh score was also higher for the iHCC cohort compared to pkHCC patients, both at the time of registration on the waiting list (10.0 (9.0 - 11.0) vs 5.0 (5.0 – 6.0); p < 0.001) and LT (10.0 (8.0 – 12.0) vs 5.0 (5.0 – 7.0); p < 0.001). None of the iHCC patients got Child-Pugh A score vs 76,3 % of the patients with pkHCC (p < 0.001). Child-Pugh class C cirrhosis at LT was mainly found in the iHCC cohort (55.6 % vs 6.2%; p < 0.001). No statistical difference was observed between the 2 cohorts for the level of alfa-fetoprotein, neither at time of registration nor at LT. However, des-carboxy-prothrombin (DCP) level was significantly higher at time of LT in the iHCC cohort (273.8 (228.9 - 551.1) vs 42.0 (22.5 - 96.0); p = 0.022). The time spent on the waiting list was a bit longer in the iHCC cohort but it was not statistically significant. The interval between the last imaging and the LT was longer in the iHCC cohort than in the pkHCC cohort (2.7 months (1.9 – 3.7) vs 1.0 (0.5 – 1.7); p < 0.004). Based on histological analysis, Edmondson grade II lesions were more frequently found in the iHCC cohort. However, there was no difference regarding the Milan status, the number of nodules and the microvascular invasion rate. None of the 9 iHCC patients got recurrence of HCC post-LT. Cumulated recurrence at 1, 3 and 5 years post-LT for pkHCC patients were respectively 3 %, 7 % and 11 %. No significant difference was observed for 1, 3 and 5-year survival rates for iHCC patients compared to pkHCC patients (respectively 100 %, 88 % and 53% vs 90 %, 87 % and 68 %; p = 0.565).

Conclusions: In our cohort, 12% of the patients transplanted for decompensated cirrhosis had a diagnosis of iHCC. However, iHCC influenced neither the neoplastic recurrence rate nor the survival rate compared to pkHCC patients. iHCC lesions were predominantly found in alcoholic decompensated cirrhosis with elevated DCP level at time of LT.

- A11 –

VALIDATION OF A GLYCOMICS-BASED TEST ASSOCIATED WITH RISK OF HCC DEVELOPMENT IN CIRRHOSIS. X. Verhelst (1), L. Meuris (2), R. Colman (3), A. Geerts (4), A. Van Hecke (2), N. Callewaert (5), H. Van Vlierberghe (4) / [1] Ghent University Hospital, Ghent, Belgium, Department of Gastroenteroly and Hepatology, [2] VIB, Gent, Belgium, VIB-Ugent Center for Medical Biotechnology, [3] Universiteit Gent, Gent , Belgium, Biostatistics Unit, Department of Public Health and Primary Care, [4] University Hospital Ghent (UZ Gent), Gent, Belgium, Department of Gastroenterology and Hepatology, [5] VIB, Gent, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Cirrhosis is the main risk factor for the development of hepatocellular carcinoma (HCC). Six-monthly screening with ultrasound is advocated for the surveillance of cirrhotic patients. We recently showed that a glycomics-based test (GlycoCirrhoTest [GCT]) can provide additional information regarding the risk of HCC development in cirrhotic patients.

Aim: The aim of this study is to provide an independent clinical validation of the GCT for the assessment of the risk of HCC development in cirrhosis.

Methods: Validation study on serum samples of patients with established compensated cirrhosis (CHILD Pugh A&B) in a tertiary liver center. Serum N-glycan profiling was performed and GCT was calculated at baseline using DNA sequencer assisted fluorophore assisted capillary electrophoresis. During the follow up period, patients were screened for the presence of HCC every 6 months with ultrasound and alpha foeto protein (AFP) measurements.

Results: A total of 198 cirrhotic patients were followed during a median follow up time of 7 years. Twenty-nine patients developed HCC and one died during follow up. At baseline, the mean GCT value was significantly higher in patients who developed HCC within 3 and 5 years compared to patients who did not develop HCC (Welch's t-test, p-value 3

years: 0.034, 5 years: 0.022). Hazard ratio for HCC development at 5 years based on GCT was 2.9 (95% CI, 1.2 – 7.0). Applying the same cut-off as from the proof-of-concept study (0.2), the negative predictive value of GCT for HCC development was 98.9%. GCT is based on changes in serum protein glycosylation related to cirrhosis nodularity and malignant transformation.
Conclusions: This independent validation study confirms that GCT is a glycomics-based test that provides additional information for risk assessment of HCC development in cirrhosis. This information could be used to develop personalised HCC screening programs in cirrhotic patients according to the value of GCT. Moreover, refocusing of the screening resources to the reduced number of cirrhosis patients who truly are at elevated risk for developing HCC may result in earlier detection of more HCC cases, for instance by making contrast-enhanced MRI screening cost-effective.

- A12 -

TACROLIMUS DRUG EXPOSURE LEVEL IN THE FIRST YEAR AFTER LIVER TRANSPLANTATION IS AN INDEPENDENT RISK FACTOR FOR DE NOVO MALIGNANCY IN PATIENTS TRANSPLANTED FOR ALCOHOL-RELATED LIVER DISEASE. B. Vanlerberghe (1), H. Van Malenstein (2), M. Sainz-Barriga (3), D. Monbaliu (3), S. Van Der Merwe (2), J. Pirenne (3), F. Nevens (2), J. Verbeek (2) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] University Hospitals Leuven, Belgium, Department of Gastroenterology and Hepatology, [3] University Hospitals Leuven, Belgium, Abdominal Transplantation Surgery.

Introduction: De novo malignancy (DNM) is a major cause of mortality in patients undergoing liver transplantation (LTx) for alcohol-related liver disease (ALD). Immunosuppression protocol may influence the risk of DNM, but evidence is conflicting.
Aim: To assess the DNM risk of different types of immunosuppression and tacrolimus drug exposure levels (TDEL) in patients transplanted for ALD.
Methods: We retrospectively analyzed all patients transplanted for ALD between 1990 and October 2016 at our center (n=317). Patients with a post-LTx follow-up of <12 months (n=22), a DNM in the 1st year post-LTx (n=11) or switch of calcineurin-inhibitor type in the 1st year post-LTx (n=20) were excluded. Total TDEL was calculated by area under the curve of trough levels (in µg/L) in the 1st year post-LTx. Risk factors for DNM (excluding non-melanoma skin cancers) within 5 years after LTx were analyzed by Cox regression (presented as hazard ratio (HR) with 95% confidence interval). Furthermore, we analyzed the incidence of DNM within 5 years post-LTx and TDEL over different eras: 1998-2002, 2003-2007, 2008-2012 and 2013-2016.
Results: 264 patients were included. Median age at LTx was 59.0 years (interquartile range (IQR): 54.0-64.0), 206 (78%) patients were male, and median follow-up post-LTx was 95.5 months (IQR: 65.0-151.8). 222 patients received tacrolimus and 42 cyclosporin in the 1st year post-LTx. TDEL was known for 212 patients, mean trough level was 7.44 (95%CI: 7.22-7.66). 184 (69.7%) patients had a smoking history (ever smoking), of which 80 (30.3%) smoked until LTx and 63 (23.9%) post-LTx. 35 patients developed 36 DNMs within 5 years post-LTx (lung (n=9), oro-pharyngolaryngeal (n=9), bladder (n= 3), esophageal (n= 3) and other (n=12)). In multivariate analysis, type of immunosuppression (tacrolimus vs. cyclosporin and mycophenolic acid vs. azathioprine), any alcohol relapse and sex were not associated with a higher DNM risk, in contrast with age at LTx (p = .003) and smoking history (p = .014). In patients on tacrolimus, TDEL was higher in those with than those without a DNM (8.35 (95%CI: 7.73-8.97) vs. 7.32 µg/L (95%CI: 7.09-7.55), p = .003). In multivariate analysis, a higher TDEL (HR: 1.540 (1.208-1.962); p < .001), age (HR: 1.120 (1.054-1.190); p < .001) and smoking history (HR: 11.427 (1.541-84.715); p = .017) were independent risk factors for DNM. TDEL decreased over the respective eras: 8.85 (95%CI: 8.14-9.55), 8.10 (95%CI: 7.67-8.53), 7.22 (95%CI: 6.87-7.57) to 6.62 µg/L (95%CI: 6.32-6.92) (p < .001). In parallel, DNM incidence also declined over the respective eras (30.43%, 8.77%, 9.23%, 10.45%; p = .033), despite an increase in median age (56.0 (IQR: 53.0-60.0), 59.0 (IQR: 53.5-62.0), 59.0 (IQR: 54.50-65.50), 62.0 (IQR: 54.0-66.0) years); p = .022).
Conclusions: Tacrolimus dose minimization in the 1st year after LTx might be an approach to lower the risk of DNM in patients transplanted for ALD and should be investigated in prospective trials.

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BENEFIT OF REGULAR SCREENING FOR HEPATITIS DELTA AND SUBSEQUENT CIRRHOSIS AMONG CHRONIC HEPATITIS B CARRIERS. T. Serste (1), H. Njimi (2), M. Nkuize (3), M. Van Gossum (3), P. Eisendrath (3), J. Mulkay (3) / [1] CHU Saint-Pierre, Brussels, Belgium, Hepato Gastro, [2] Erasme Hospital, Brussels, Belgium, Intensive Care, [3] CHU Saint-Pierre, Brussels, Belgium, Hepatogastroenterology.

Introduction: There is general acceptance that about 5% of patients with chronic Hepatitis B Surface Antigen (HBs Ag) are infected with Hepatitis Delta Virus (HDV), but the exact prevalence of this infection is underestimated due to the lack of routine screening for anti-HDV antibodies (HDV Ab) in HBs Ag positive patients. HDV infection is considered the most severe form of viral hepatitis and the regular assessment for fibrosis and screening for cirrhosis is therefore recommended in these patients.
Aim: We aimed to assess the benefit of a systematic annual screening strategy for HDV in a population of HBs Ag chronic carriers. We also reported the clinical impact of a systematic and repeated screening for cirrhosis during follow-up in these patients.
Methods: This was a single center (CHU Saint Pierre, Brussels) study based on a retrospective analysis of a prospective database. Between January 2014 and October 2021, we tested all chronic HBs Ag positive patients for HDV Ab with a systematic and annually repeated screening policy. Each HDV Ab positive patient underwent a repeated non-invasive evaluation of the fibrosis progression by elastometry (Fibroscan ©). We quantified the viral load of HDV in HDV Ab positive patients with HDV RNA PCR. The characteristics of patients with a detectable HDV RNA (group 1) were compared to patients with undetectable HDV RNA (group 2).
Results: Six hundred and ten (610) chronic HBs Ag positive patients were identified during the study period. Five hundred and forty-four (544) patients were tested at least once for HDV Ab while the annual HDV Ab screening could be done in 534 patients. This highlighted 67 (12.3%) patients with positive HDV Ab, including 7 cases diagnosed as HDV superinfections in initially HDV Ab negative patients. Among these 67 HDV Ab positive patients, the median age was 38 years (range 20-73), 37 (55.2%) were men, 35 (52.2%) were Caucasians and 30 (44.8%) were Africans. The level of GPT was 64 IU / mL (12-374). The median follow-up time was 4.0 years (0-15.8). Cirrhosis was initially diagnosed in HDV Ab positive patients at the beginning of the follow-up in 11/ 67(16.4%) and during the follow-up in 8 patients (11.9%). The cumulative incidence of cirrhosis in HDV Ab positive patients at one year and 5 years of follow-up was 19.4 % (95%CI 9.4-28.3) and 25.0% (95%CI 12.4-35.7) respectively. The HDV RNA PCR was performed in 57/67 HDV Ab positive patients, 27 (47.3%) were detectable. Patients with detectable HDV RNA PCR (group 1) had a significantly higher GPT level (93 IU versus 58 IU / mL, p = 0.023) and were more frequently of Caucasian origin (74.1% versus 23.3%, p≤0.0001) than undetectable patients (group 2). The cumulative incidence of cirrhosis at 1 year of follow-up was 33.3% (95%CI 13.0-48.9) in group 1 and 10.0% (95%CI 0.1-20.1) in group 2 (p = 0.032). At 5 years of follow-up, the cumulative incidence of cirrhosis was 38.1% (95%CI 16.1-54.3) in group 1 and 10.0% (95%CI 0.1-20.1) in group 2 (p = 0.023).
Conclusions: A systematic and repeated screening strategy for hepatitis delta in patients with chronic HBs Ag patients enables the identification of a high prevalence of HDV Ab, much higher than previous estimates. Regular assessment for cirrhosis in HDV Ab positive patient is effective, especially in patients with detectable HDV RNA.

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PRETRANSPLANT CHANGES IN SERUM PROTEIN GLYCOSYLATION RELATE TO RISK OF HCC RECURRENCE AFTER LIVER TRANSPLANTATION AND PROVIDE A POTENTIAL PROGNOSTIC BIOMARKER: A PROOF-OF-CONCEPT STUDY. X. Verhelst (1), H. Engels (2), A. Geerts (2), A. Vanlander (3), L. Abreu De Carvalho (3), H. Degroote (2), L. Meuris (4), F. Berrevoet (3), N. Callewaert (4), H. Van Vlierberghe (2) / [1] Ghent University Hospital, Ghent, Belgium, Department of Gastroenteroly and Hepatology, [2] University Hospital Ghent (UZ Gent), Gent, Belgium, Department of Gastroenterology and Hepatology, [3] University Hospital Ghent (UZ Gent), Gent, Belgium, Department of General, Hepatobiliary and Transplant Surgery, [4] VIB, Gent, Belgium, VIB-Ugent Center for Medical Biotechnology.

Introduction: Hepatocellular carcinoma (HCC) recurrence occurs after liver transplantation in 10% of patients even if Milan criteria are respected. Tumour biology should be taken into account when assessing patients with HCC for liver transplantation. In HCC specific changes have been observed in protein glycosylation that are involved in cancerogenesis and metastasis. However, the role of protein glycosylation in HCC recurrence after liver transplantation has not been studied.
Aim: The goal of this study was to assess the risk of HCC recurrence after liver transplantation, according to changes in serum protein glycosylation before liver transplantation.
Methods: A prospective study was performed in patients receiving liver transplantation in a large liver transplant hospital between 2 July 2011 and 24 September 2018. The whole serum protein N-glycan profile was assessed using DNA sequencer assisted fluorophore assisted capillary electrophoresis, using a robust and validated high-throughput protocol. For every sample, 13 glycans were quantified. Patients were followed until HCC recurrence or death. Specific changes in serum protein glycosylation profiles were searched for in patients with HCC recurrence compared to patients without recurrence. Multivariate analysis and survival analysis were used as appropriate.
Results: In this cohort of 225 consecutive liver transplant patients, 76 patients (M:63/F:13) suffered from HCC before transplantation. Main etiologies of liver disease were alcoholic liver disease (47.4%), HCV infection (21.1%) and NASH (15.8%). Eight patients (10.5%) developed HCC recurrence after a median follow up time of 9.5 months after liver transplantation. In this cohort 74 patients (97%) fulfilled Milan criteria before liver transplantation. Based on the analysis of the explant liver, 85.5% fulfilled the Milan criteria. Significant differences in the relative abundance of 5 serum glycans were present in patients with HCC recurrence compared to patients without HCC recurrence (Cox regression analysis). Based on these changes, a composite biomarker was developed (GlycoHCCRecurrenceScore). This score

integrates an increased presence of triantennary glycans with and without branch and core fucosylation (NA3, NA3Fc and NA3Fbc) and a decreased presence of undergalactosylated glycans NGA2F and NGA2FB in patients with HCC recurrence. This composite biomarker panel shows an AUC of 0.855 (p=0.001; 95% CI 0.731-0.979) for association with HCC recurrence. Using an optimized cut-off (-4.24), this composite biomarker shows a sensitivity of 87.5% and specificity of 67.6%. Only 2.1% of patients with a value below this cut-off showed HCC recurrence, compared to 24.1% of patients with values above this cut-off (p=0.011). Positive predictive value was 72.98% and negative predictive value 84.39%. In a univariate cox regression analysis other factors related to HCC recurrence in this cohort were diameter of the largest lesion before liver transplantation and the presence of perineural or lymphovascular invasion on the explant liver. In a multivariate analysis, the biomarker panel showed an independent relation with HCC recurrence (HR 1.931; p=0.008:1.184-3.149).
Conclusions: In this proof-of-concept study, a glycomics based serum biomarker panel is strongly associated with tumor recurrence in a cohort of liver transplant patients with HCC, even if adhering to Milan criteria. In a multivariate analysis, this biomarker was the only pretransplant discriminative parameter of HCC recurrence in this cohort. The biomarker panel could potentially increase the prediction of HCC recurrence and improve allocation strategies in liver transplant candidates with HCC.

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ABSTINENCE IS ASSOCIATED WITH BETTER OUTCOME IN PATIENTS WITH ALCOHOL-RELATED HEPATOCELLULAR CARCINOMA. A. Donati (1), J. Henrion (2), M. Regnier (3), P. Deltenre (4), A. Marot (5) / [1] Centre Hospitalier Universitaire Mont-Godinne, Belgium, Gastroenterology and Hepatology, [2] Centres Hospitaliers Jolimont, Belgium, Gastroenterology and Hepatology, [3] Centre Hospitalier Universitaire Mont-Godinne, Belgium, Department of biostatistics, [4] Clinique Saint-luc Bouge, Namur, Belgium, Gastroenterology and Hepatology, [5] Centre Hospitalier Universitaire Mont-Godinne, Belgium, Gastro-enterology and Hepatology.

Introduction: Data suggest that patients with alcohol-related hepatocellular carcinoma (HCC) have a reduced survival as compared to those with nonalcohol-related HCC. The role of abstinence in this setting in unknown.
Aim: We aimed to compare access to treatment and prognosis of patients with alcohol-related HCC and nonalcohol-related HCC and to evaluate the impact of abstinence.
Methods: All patients with HCC were retrospectively included in a single center during a 23-year period. Abstinence was defined as discontinuation of alcohol consumption at least 3 months before HCC diagnosis. Treatment by resection, ablation, and liver transplantation were considered curative. Multivariate Fine and Gray proportional hazards models were used to identify factors associated with 5-year overall mortality after adjustment for the lead-time bias. A logistic regression model was used to identify factors associated with access to curative treatment.
Results: 200 patients were included, 114 (57%) with nonalcohol-related HCC and 86 (43%) with alcohol-related HCC of whom 35 were abstainers and 51 were consumers. All of them had a cirrhosis. During a median follow-up of 14 months (95%CI: 11-16), 12 patients were transplanted and 156 died. At HCC diagnosis, consumers were younger as compared to abstainers and nonalcoholic patients (59 vs. 63 vs. 68 years, p=0.001), had a worse liver function (MELD score: 11 vs. 10 vs. 8, p=0.01, Child-Pugh score: 6 vs. 5 vs. 5, p=0.02), were less likely to be screened for HCC (33% vs. 74% vs. 51%, p<0.001) and had more frequently a metastatic disease (16% vs. 0% vs 6%, p=0.02). After adjustment for the lead-time bias, the 5-year cumulative incidence rates of overall death were significantly lower in abstainers than in consumers and in non-alcoholic patients (51.5% vs. 78.4% vs. 80.5%, respectively, p=0.04). In multivariate analyses, while abstainers were significantly associated with lower overall mortality as compared to consumers (HR: 0.47, 95% CI 0.28 – 0.80, p=0.005), patients with nonalcohol-related cirrhosis and consumers had similar overall mortality (HR: 0.86, 95% CI 0.60 – 1.24, p=0.4). The proportion of patients who received a curative treatment was 65% in abstainers, 44% in consumers and 57% in nonalcoholic patients (p=0.1). In multivariate analyses, preserved liver function (Child A vs. B/C, OR: 3.10 95% CI 1.58 – 6.26, p=0.001) and adherence to a screening program (OR: 4.96, 95% CI 2.50 – 10.15, p<0.001) were the only two factors associated with a better accessibility to curative treatment.
Conclusions: Abstinence improves the outcome of patients with alcohol-related HCC because of better liver function, less advanced tumour disease and better adherence to screening.

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THE EVOLVING PATTERN OF HEPATOCELLULAR CARCINOMA IN A GENERAL HOSPITAL FROM CENTRAL BELGIUM …THE HISTORY OF OUR REGION MADE THE DIFFERENCE! E. Kaze (1), J. Henrion (1) / [1] Centres Hospitaliers Jolimont, Belgium, Gastroenterology and hepatology.

Introduction: The epidemiology of cirrhosis has changed over the last two decades in our institution.
Aim: The aim of this study was to assess whether the epidemiology and clinical presentation of hepatocellular carcinoma (HCC) occurring in cirrhosis has also changed during the last 25 years.
Methods: From January 1995 to December 2016, 1070 patients with cirrhosis who attended the outpatient's liver clinics of our institution were consecutively included in a registry and invited to participate in a surveillance program for HCC. They were separated into 2 cohorts collected during the same time period (11 years) but eleven years apart: the cohort 1, patients included in the registry from January 1995 to December 2005 (n = 504) and the cohort 2, patients included from January 2006 to December 2016 (n= 566). The characteristics of HCC observed in both cohorts were retrospectively assessed until December 2009 for cohort 1 and December 2020 for cohort 2 in order to have the same duration of follow-up (4-15 years) for each cohort.
Results: Both cohorts of cirrhosis were comparable concerning gender, age and Child-Pugh score at inclusion in the registry. By contrast, they differed concerning the etiology of cirrhosis. In both cohorts, alcohol-related cirrhosis accounted for around 60% of cases, but HCV- and MAFLD-related cirrhosis accounted for 26% and 7% in the first cohort and for 13% and 14% in the second, respectively (p<0.001). HCC were observed in 89 patients (HCC group 1) in the cohort 1 (18%) compared to 73 patients (HCC group 2) in the cohort 2 (13%) (p=0.03). Concerning the presentation of HCC at the time of diagnosis, no differences were found between the groups about the age at diagnosis of HCC, the test which alerted on the presence of HCC, the extension of HCC on medical imaging, and the BCLC staging. Moreover, there were no differences for the proportion of HCC diagnosed concomitantly to the diagnosis of cirrhosis or incidentally during follow-up (incident HCC, 65% in HCC group 1 versus 66% in HCC group 2) as well as the proportion of HCC diagnosed inside or outside the surveillance program (50.5 % of HCC diagnosed within the surveillance program in HCC group 1 versus 52 % in HCC group 2). By contrast, the etiology of the underlying cirrhosis differed significantly between the groups, HCV-related cirrhosis being the main cause of HCC in the first group (HCC group 1: alcohol 27 %, HCV 53 %, MAFLD 10 %, other 10 % versus HCC group 2: alcohol 60 %, HCV 18 %, MAFLD 11 %, other 11 %). Another difference was the ethnic origin of the patients. In HCV-related HCC in group 1, the proportion of patients from Italian origin (47%) exceeded the proportion of patients from Belgian origin (43%) while they were more Belgian patients with HCV-related HCC in group 2 (Italian 31%, Belgian 62%).
Conclusions: 1/ In this study covering 25 years of HCC in our hospital, the only change was the decrease of HCV-related HCC. In HCC group 1, HCV infection was the main cause of the underlying cirrhosis before alcohol. This high proportion of HCV-related HCC in the first group may be explained by the high proportion of elderly patients of Italian origin in our region 25 years ago. Indeed, in the 1950s, an agreement was established between Belgium and Italy for immigration of Italian workers for coal mining. The epidemic of HCV infection was more widespread and began earlier in Italy. Consequently, in the 1990s we observed numerous HCV-related cirrhosis in elderly patients born in Italy. This population has now, almost disappeared. 2/ The higher prevalence of HCV-related cirrhosis in cohort 1 could explain the higher emergence of HCC in this cohort. 3/ MAFLD-related cirrhosis has increased, but not yet MAFLD-related HCC.

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POINT OF CARE SCREENING TESTS FOR HEPATITIS B AND COMMITMENT OF A DEDICATED NURSE LEAD TO SUCCESSFUL LINKAGE TO CARE OF ETHNIC MINORITIES. A. Vanderlinden (1), E. Ho (2), L. Govaerts (3), B. De Fooz (3), P. Van Damme (4), P. Michielsen (2), T. Vanwolleghem (2) / [1] University of Antwerp/ Antwerp University Hospital, Edegem, Belgium, Gastroenterology Hepatology, [2] Universiteit Antwerpen / Antwerp University Hospital, Wilrijk (Antwerpen), Belgium, Gastroenterology Hepatology, [3] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology Hepatology, [4] Vaxinfectio - University of Antwerp, Antwerpen, Belgium, Vaxinfectio.

Introduction: Hepatitis B virus (HBV) is a major global health issue. Recently, the WHO set new targets to eliminate viral hepatitis by 2030 with the emphasis on raising awareness, scaling up screenings and treatment services. Belgium is a low endemic country, with an estimated HBsAg seroprevalence of 0.66% (95% CI 0.51–0.84) for Flanders in 2003. In low endemic countries, HBsAg screening in migrants is cost-effective to reduce the burden of HBV infection, but the linkage to care remains a challenge. Our group previously showed that outreach screenings for HBV using point of care tests (POCT) compared to venepunctures resulted in a 2.5 times higher linkage to care in an Asian migrant population in Belgium.
Aim: A primary objective was to examine whether the observed improved linkage to care using POCT is influenced by ethnicity using outreach POCT screening among different ethnic groups (Middle East, Sub-Saharan Africa and Asia) and the commitment of a dedicated screening nurse. A secondary objective, was to compare the reported HBsAg seroprevalence in the general Flemish population versus those estimated for ethnic minorities.
Methods: Opportunistic screenings using finger prick Vikia HBsAg tests (Biomérieux SA, Marcy-l'Etoile, France) were performed at municipal integration classes in Antwerp ("Atlas") between 11/2017 and 03/2021. If tested positive, an appointment was given immediately at the outpatient hepatology clinic for follow-up and confirmation of HBsAg positivity in blood. A strict follow up of HBV infected patients was guaranteed by a dedicated nurse who contacted them via phone, Whatsapp or by making home visits before the patients' visit to the hospital. Ethnicity was based on the participants' country of birth. Linkage to care was described as having received medical care from a hepatologist, a blood test and an abdominal ultrasound.

Results: A total of 521 persons with different ethnicities were serologically screened using POCT tests. Overall, seroprevalence for HBsAg was 3.45% (18/521). For Africa, Middle-East and Asia the seroprevalence was respectively: 3.20% (4/125), 4.64% (13/280) and 0.86% (1/116). The prevalence of hepatitis B is higher among all ethnic minorities combined compared to general Flemish population with a HBsAg seroprevalence of 0.66% in 2003 ($p<0.0001$), and thus supports targeted HBsAg screening in Flanders. Our previous study showed that 34.38% (11/32) of HBV infected Asian migrants in Antwerp were linked to care using venepuncture as screening method. This was used as baseline to compare the linkage of care using POCT among different ethnicities. Linkage to care is significantly higher with POCT and a dedicated nurse in Sub-Saharan African ($p=0.023$) and Middle-Eastern ($p<0.0001$) migrants in comparison with venepuncture. No significant difference in linkage to care using POCT compared to venepuncture in the Asian group was observed ($p=0.36$). Since all HBsAg positives were linked to care, the ethnicity did not affect linkage to care. Despite COVID-19 pandemics, linkage to care remains high using POCT and through the commitment of a dedicated nurse who strictly followed up the patients. However, the time frame between screening and the first hospital visit is significantly higher ($p=0.0049$) during the COVID-19 pandemic than in the pre-pandemic period. Among the HBsAg seropositives in the identified patients by POCT, 22.22% (4/18), 83.33% (15/18) and 22.22% (4/18) met criteria for HCC surveillance, transmission risk and treatment indication respectively. Noteworthy was that 16,67% (3/18) of the migrants had experienced hepatitis D infection. This demonstrates the usefulness of screening in ethnic minorities to reduce the burden of HBV infection.
Conclusions: To meet WHO's goal of eliminating hepatitis B by 2030, it is important to screen ethnic minorities as the prevalence is higher than in the Flemish population. Screening campaigns based on POCT and the help of a dedicated nurse are urgently warranted as this leads to a successful linkage to care in ethnic minorities compared to standard venepunctures.

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EXCELLENT OUTCOME AND VACCINATION RATE IN PATIENTS WITH AUTOIMMUNE HEPATITIS DURING THE COVID-19 PANDEMIC. H. De Sutter (1), H. Degroote (1), H. Van Vlierberghe (1), X. Verhelst (1) / [1] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Autoimmune hepatitis (AIH) is a rare autoimmune liver disease. The cornerstone of treatment is the use of immunosuppressive drugs, which might lead to adverse outcome when patients are infected with the SARS-CoV-2 virus.
Aim: 1. Assess outcome in AIH patients infected with SARS-CoV-2 virus (infection, need for hospitalization, liver failure, death) 2. Assess ideas and concerns in AIH patients regarding the need for vaccination, assess vaccination rates and assess adherence to preventive measures for SARS-CoV-2 virus.
Methods: This was a monocentric study in a large tertiary center specialized in AIH. We carried out a phone-based questionnaire. The questionnaire addressed seven pillars in the COVID-19 pandemic: presence of COVID-19 related symptoms (fever, respiratory symptoms, anosmia), testing for COVID-19, developing COVID-19 disease, need for hospitalization, adherence to the national guidelines for the prevention of COVID-19 infection, adherence to their immunosuppressive treatment and vaccination for COVID-19. The phone-based questionnaire was performed between 25/8/2021 and 18/11/2021. Only the period between September 2020 and November 2021 was taken into consideration when answering the questions. Medical data (hospitalization etc.) were retrieved from the electronic medical records.
Results: Ninety-two participants (31,5% males; 68,5% females) were included. In the period between September 2020 and November 2021, forty-eight patients (52,2%) showed one or more COVID-19 related symptoms. Seventy-one patients (77,2%) were tested for a COVID-19 infection by PCR. Most frequent reasons for testing were: hospitalization, presence of symptoms and high-risk contact(s). Seven patients (9,9%) confirmed positive for COVID-19 infection at least once. Two patients (2,2%) needed hospitalization for severe COVID-19 disease, of which one patient stayed in Intensive Care due to severe respiratory symptoms. Eighteen patients (19,2%) visited mass events (more than hundred persons). Ten patients (10,9%) didn't allow any visitors in their houses since the beginning of the COVID-19 pandemic. Seven patients (7,6%) considered stopping their immunosuppressive treatment. Two patients (2,2%) have effectively stopped their treatment despite medical advice to continue treatment. The majority (94,6%) of the patients are vaccinated against COVID-19. Sixty-three patients (72,4%) got the Pfizer-BioNTech COVID-19 vaccine, seventeen patients (19,5%) the Oxford AstraZeneca COVID-19 vaccine and seven patients (8,0%) the Moderna COVID-19 vaccine. Thirty-six patients (41,4%) showed side effect from their vaccine. Most frequent side effects were: fatigue, myalgia and general malaise.
Conclusions: Half of the patients with AIH developed symptoms compatible with a COVID-19 infection. The patients showed a limited infection ratio. A minority of patients needed hospitalization due to COVID-19 disease. The patients showed an excellent adherence to the national guidelines for the prevention of COVID-19 infection. The majority of the patients continued their immunosuppressive treatment. This supports the idea that immunosuppressive treatment should not be stopped in patients with AIH, even during the COVID-19 pandemic. The vaccination rate among the patients in this cohort was excellent.

IS INSULIN RESISTANCE THE PREDISPOSING FACTOR FOR FATTY LIVER DISEASE IN TYPE 1 DIABETES? J. Mertens (1), M. Spinhoven (2), E. Dirinck (3), L. Vonghia (1), C. De Block (3), S. Francque (1) / [1] University of Antwerp/Antwerp University Hospital, Edegem, Belgium, Gastroenterology and Hepatology, [2] University of Antwerp/ Antwerp University Hospital, Edegem, Belgium, Radiology, [3] University of Antwerp/Antwerp University Hospital, Edegem, Belgium, Endocrinology, Diabetology and Metabolism.

Introduction: NAFLD is globally increasing due to its association with overweight, metabolic syndrome, and type 2 diabetes. Overweight and metabolic syndrome are increasingly prevalent in type 1 diabetes (T1D) leading to a potential increase in NAFLD cases in these individuals. However, the epidemiology of NAFLD in T1D remains uncertain. Furthermore, the etiology of fatty liver disease in T1D is unclear, due to several potential pathways leading to, but also seemingly protecting from steatosis in T1D.
Aim: This cross-sectional study investigated the possible association between liver fat content (LFC), NAFLD, and insulin resistance (IR) in individuals with T1D.
Methods: Patients with T1D who consented underwent magnetic resonance spectroscopy (MRS) to determine LFC based on three separate regions of interest. The estimated glucose disposal rate (eGDR) was calculated as an index of insulin sensitivity based on the presence of hypertension, the waist circumference, and the HbA1c level (%). The eGDR is validated against the euglycaemic clamp technique, which is the gold standard to evaluate IR in subjects with T1D. A mean liver fat content ≥ 6.0% on MRS was considered diagnostic for NAFLD (reference standard). Secondary causes of liver steatosis were ruled out in all.
Results: Seventy-eight subjects with T1D were included. The mean age was 59 ± 17 years, mean body mass index (BMI) was 27.6 ± 5.0 kg/m2, mean waist circumference was 87 ± 13 cm in females and 99 ± 12 cm in males, and hypertension was present in 63% of cases (based on the definition of the metabolic syndrome). Mean LFC based on MRS was 4.3 ± 4.0 %, NAFLD was present in 11 (14%) subjects. Mean Hb A1c was 7.4 ± 1.2 % indicating overall good glycaemic control. The mean eGDR was 6.4 ± 2.5 mg/kg/min. Distributed over tertiles, 40% of subjects had a low eGDR indicating significant insulin resistance. NAFLD distribution was significantly different across tertiles with 64% (7/11) of NAFLD cases in the lowest tertile indicating insulin resistance, and 0% of cases in the highest tertile indicating insulin sensitivity ($p = 0.038$). Linear regression showed a weak correlation between eGDR and LFC (r: -0.277, B:-0.442, 95% CI: -(0.792 - 0.91), $p = 0.014$). In logistic regression, NAFLD was associated with the eGDR as a continuous variable (OR 0.63, 95% CI 0.42 - 0.95, $p = 0.029$) in a model including BMI, age, and gender.
Conclusions: This preliminary data show that IR, as indexed by the eGDR, is associated with LFC and the presence of NAFLD in individuals with T1D. More studies are needed to further elucidate the specific factors playing a role in the etiology of NAFLD in individuals with T1D.

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ASSESSMENT OF A TRANSIENT ELASTOGRAPHY IN PREDICTING THE GRAFT FIBROSIS AFTER LIVER TRANSPLANTATION AND VALIDATION OF THE VENTURI SCORE IN AN ADULT POPULATION. C. Dumont (1), N. Lanthier (1), S. Iesari (2), G. Henin (1), E. Bonaccorsi-Riani (3), O. Ciccarelli (3), L. Coubeau (3), P. Baldin (4), S. Aydin (4), G. Dahlqvist (1) / [1] Clin universitaires St-Luc, UCL, Brussels, Belgium, Department of Gastroenterology and Hepatology, [2] Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Italy, Department of General surgery and Kidney Transplantation, [3] Clin universitaires St-Luc, UCL, Brussels, Belgium, Department of General Surgery and Abdominal Transplantation, [4] Clin universitaires St-Luc, UCL, Brussels, Belgium, Department of Pathology.

Introduction: Progressive liver graft fibrosis is a cause of graft failure and late death in the follow-up of transplant patients. Early detection of liver graft fibrosis is crucial to improve survival of transplant patients. Liver biopsy is still the gold standard to detect fibrosis of the graft but is an invasive, costly and not complication-free procedure. Transient elastography (TE) might measure graft fibrosis but data are lacking for this population. Regarding the assessment of fibrosis, the Metavir score is still used, but not designed for a transplant cohort. The liver allograft fibrosis semiquantitative scoring system (LAFSc or Venturi Score) was designed and validated to assess the fibrosis in a pediatric transplant population better than with the Metavir score.
Aim: Our aims are to determinate if TE could be correlated to histological scores and to validate LAFSc in an adult population.
Methods: We included 52 liver transplant recipients followed-up at our institution who underwent per-protocol liver biopsies between 02/2021 and 10/2021. The biopsy was a 6-months, 1-year, 5-, 10-, 15- or 20-years follow-up procedure, depending on the date of the transplantation. A TE (FibroScan®) was performed before each protocol liver biopsy. With TE, we measured liver stiffness and liver steatosis severity assessed by the controlled attenuation parameter (CAP). Each biopsy sample was examined in the department of pathology of our institution, by one experienced pathologist. Graft fibrosis was classified according to Metavir score and LAFSc. The association between Metavir and LAFSc, and between histological scores and TE was tested through the Spearman's rank correlation coefficient (rho), which was

reported alongside the 95% confidence interval (CI). The relationship between the different scores was modelled through linear regressions and r^2 were reported. All tests were two-tailed. Significance was retained at $p < 0.05$. Analyses were run with GraphPad Prism 8.0 (GraphPad Software Inc., San Diego, CA-US).
Results: 62% of the patients were male, median age was 59. Mean BMI was 27 kg/m². The main initial etiology was alcohol-related cirrhosis (21%). 35% of the patients had hepatocellular carcinoma. Median stiffness, CAP and IQR/med were 6.4 kPa, 234 dB/m and 16% respectively. We found out a positive correlation between LAFSc and TE (kPa) (rho = 0.35, CI = 0.07-0.58, p = 0.01, r^2= 0.11, p = 0.02). We observed a positive correlation between Metavir and TE (kPa) (rho = 0.31, CI = 0.02-0.55, p = 0.03, r^2= 0.12, p = 0.02). We found out a positive correlation between Metavir and LAFSc (rho = 0.66, CI = 0.47-0.80, p < 0.01). LAFSc explained 51% of the variation in Metavir ($r^2 = 0.51$, $p < 0.01$). There was no correlation between CAP and histologically graded steatosis (rho = 0.29, CI = -0.01-0.54, p = 0.05, $r^2 = 0.04$, p = 0.16)
Conclusions: We found a strong correlation between Metavir and LAFSc in grading fibrosis, a weak correlation between TE values and histological fibrosis scores and no correlation between CAP and histological steatosis. This suggests that LAFSc is a valuable scoring system of fibrosis for adult recipients and warrants further research to determine whether it better predicts the graft fate.

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PROSPECTIVE VALIDATION OF THE POLYCYSTIC LIVER DISEASE COMPLAINT-SPECIFIC ASSESSMENT (POLCA) SCORE: INFLUENCE OF MENOPAUSE AND SOMATOSTATIN-ANALOGUES. A. Billiet (1), F. Temmerman (1), W. Coudyzer (2), N. Van Den Ende (1), I. Colle (3), S. Francque (4), H. Thien Anh (5), S. De Maeght (6), F. Janssens (7), H. Orlent (8), D. Sprengers (9), J. Delwaide (10), S. Decock (11), C. De Vloo (12), S. Van Der Merwe (1), J. Verbeek (1), F. Nevens (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Radiology, [3] ASZ, Aalst, Belgium, Gastroenterology and Hepatology, [4] Antwerp University Hospital, Edegem, Belgium, Gastroenterology and Hepatology, [5] Université catholique de Louvain (UCLouvain), Belgium, Nefrology, [6] Grand Hopital de Charleroi, Charleroi, Belgium, Gastroenterology and Hepatology, [7] Jessa Hospital, Hasselt, Belgium, Gastroenterology and Hepatology, [8] AZ Sint-Jan Brugge-Oostende, Brugge, Belgium, Gastroenterology and Hepatology, [9] Sint Augustinus Ziekenhuis GZA, Antwerp, Belgium, Gastroenterology and Hepatology, [10] CHU Liege, Liège, Belgium, Gastroenterology and Hepatology, [11] AZ Sint-Lucas Brugge, Assebroek/ Brugge, Belgium, Gastroenterology and Hepatology, [12] AZ Delta, Roeselare, Belgium, Gastroenterology and Hepatology.

Introduction: Polycystic liver disease (PCLD) can lead to extensive hepatomegaly, often associated with severe complaints. Indication for somatostatin-analogues (SA) or liver transplantation is in part based on subjective, patient-reported symptoms. In 2014 the PCLD-complaint-specific assessment (POLCA) score was developed as a self-report instrument to objectively capture the presence and severity of disease-specific complaints (Temmerman F, J Hepatol 2014). Previous studies have shown that liver volume in PCLD tends to decrease after menopause and with use of SA.
Aim: The aim of this study was to highlight the correlation between the POLCA severity of perceived illness (SPI) score and the changes in liver volume in PCLD.
Methods: A five-year prospective multi-centric study in 21 hospitals in Belgium gathered a cohort of 266 PCLD patients. Sequential data including POLCA score, liver volumetry and the need for volume-reduction therapy were recorded. Participants were asked to complete the POLCA questionnaire, as available online (https://www.uzleuven.be/polca). Liver volume was measured using CT-volumetry and adapted as height-adjusted total liver volume (htLV). Combined liver-kidney transplant patients (n=9) were excluded. Menopause was defined as 52 years of age or more. Effect of menopause on htLV was calculated in women with consecutive volumetry, after excluding those who were receiving SA to reduce confounding.
Results: For 198 patients, serial POLCA scores were available. The study group consisted of young (54.8y ±11.3), mostly female (83%) patients with predominant autosomal dominant polycystic kidney disease (ADPKD) (63%). Median time of follow-up was 48 months. Liver volumetry was available for 96 patients, showing a median htLV of 1967ml. Overall, there was a significant correlation (Spearman's rank) between the POLCA severity of perceived illness score (POLCA SPI) and htLV (r=0.48; 0.30-0.63) and longitudinal data showed a significant correlation between the change in POLCA SPI score and the change in htLV (r=0.45; 0.26-0.61). Patients who underwent liver transplantation (n=18) had higher htLV (3607ml vs 1707ml; p<0,0001) and significantly higher results on all POLCA subscores: severity of perceived illness score (POLCA SPI) (23.5 vs 10; p<0,0001); reflux related complaints (7 vs 2; p <0,0001); impact on food intake (6 vs 2; p=0,0004); perception of enlarged liver volume (10 vs 6; p<0,0001). POLCA SPI score ≥ 16.5 predicted the need of LT with a sensitivity of 81.3% and a specificity of 88.9%. Women treated with SA (n=62) showed a decrease in htLV after 12 months (-121ml vs +74ml; p<0,0001). A significant reduction in htLV (– 80ml) by SA resulted in a decrease in POLCA SPI score (-6.0 vs +4.5; p<0,0001). In premenopausal (n=20) vs postmenopausal women (n=14) the change in htLV per year was significantly different (+152ml/y vs -6ml/y respectively; p<0,0009) and premenopausal women had higher POLCA SPI scores (13 vs 9; p=0,0050).
Conclusions: This study further demonstrates the correlation between the POLCA score and objective changes in liver volume. Menopause and treatment with SA decrease liver volume in patients with PCLD and reduce symptom burden as is reflected by the POLCA score. Our findings highlight the potential of the POLCA score as a tool for longitudinal follow-up of PCLD patients and as a guide for clinicians when evaluating the need for medical or surgical intervention.

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MURINE BILE DUCT LIGATION INDUCES LIVER FUNCTION FAILURE, NEUROMETABOLIC CHANGES AND MICROGLIAL ACTIVATION INDICATIVE OF HEPATIC ENCEPHALOPATHY. W. Claeys (1), L. Van Hoecke (2), A. Geerts (1), X. Verhelst (1), H. Van Vlierberghe (1), S. Lefere (1), H. Degroote (1), G. Van Imschoot (2), E. Van Wonterghem (2), R. Vandenbroucke (2), C. Van Steenkiste (3) / [1] Ghent University, Ghent, Belgium, Hepatology Research Unit, Liver Research Center Ghent, [2] VIB Center for Inflammation Research, Gent, Belgium, Barriers in Inflammation, [3] University of Antwerp, Antwerp, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Hepatic Encephalopathy (HE) is a frequent complication of liver cirrhosis, associated with poor outcomes. Current understanding is that hyperammonemia and systemic inflammation synergize to induce neuropsychiatric symptoms. Validated and well-characterized murine models of chronic HE are lacking at present.
Aim: This study aims to validate murine bile duct ligation (BDL) as a model for HE in chronic liver disease. Secondly, this project aims to describe the temporal evolution of the key characteristics of HE within this model.
Methods: Male C57Bl/6j mice underwent BDL or sham surgery (n=15/group/timepoint) and were sacrificed 7, 14, 21 and 28 days after induction. Standardized motor function tests (open field test, difficult beam traversal) were performed. Plasma samples were collected for liver enzyme and cytokine assessment. Liver samples were isolated for histology. Targeted metabolomics (LC-MS/MS) for amino acids, bile acids and energy metabolites were performed on cerebrospinal fluid (CSF). Brain samples were taken for immunostainings and cytokine profiling. In a separate experiment, mice were injected with 4kDa FITC-Dextran 15 min before sacrifice to assess blood-brain barrier (BBB) permeability changes. All analyses are comparisons to sham controls.
Results: BDL induces early changes in motor function, with increased beam traversal time (+60%, p=0.0056 at day 7) and decreased travelling distance in the open field (-71%, p<0.0001 at day 14). BDL induces liver injury (increased ALT and AST, all p<0.0001) and liver function failure (decreased albumin, p=0.0354 at 14 days). Bridging fibrosis is apparent in all mice, 28 days after induction. Plasma ammonia levels progressively increase in BDL mice, reaching a plateau at 21 days (81.58 vs. 169.5 µMol/L, p=0.0012). Targeted CSF metabolomics show a steady increase in glutamine levels in BDL mice, mirroring plasma ammonia evolution (p=0.0029 at 14 days). Additionally, glutamate (p=0.0095 at 14 days) and brain osmolytes taurine (p=0.0045 at 14 days) and creatine (p=0.0192 at 14 days) transiently decrease. Interestingly, plasma ammonia correlates significantly with CSF glutamine (r=0.5076, p=0.0113). AMP is depleted at 14 days (p =0.0021), but other energy markers are not altered in BDL mice. Remarkably, taurocholic acid (p=0.0016), but also tryptophan (p=0.0084), accumulates in CSF after 7 days. Systemic inflammation is evident from 7 days, with an increase in plasma IL-6 levels (p=0.0002 at 7 days). 3D reconstructions of microglia show that cortical microglia of BDL mice exhibit decreased complexity (p=0.0052) from 14 days onward, consistent with activation. This microglial activation is accompanied by an increase in CCL2, 28 days after induction (p=0.0418). Finally, increased BBB permeability is seen 28 days after induction (p=0.0031).
Conclusions: Mice exhibit the cardinal features of HE after BDL, namely advanced chronic liver disease with hyperammonemia and increased brain glutamine. Additionally, BDL mice exhibit systemic and neuroinflammation and BBB permeability changes. BDL induces motor function changes before the development of hyperammonemia, possibly reflecting the effect of systemic inflammation or cerebral bile acid/tryptophan accumulation. Our results suggests that murine BDL can be used to model and study HE in chronic liver disease.

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SMALL CHANGES IN THE METABOLISM OF BILE ACIDS BY THE GUT MICROBIOTA ARE ASSOCIATED TO NASH PATHOGENESIS. J. Gillard (1), M. Thibaut (2), M. Roumain (3), G. Muccioli (3), A. Tailleux (4), B. Staels (4), L. Bindels (2), I. Leclercq (1) / [1] Université catholique de Louvain (UCLouvain), , Belgium, Laboratory of Hepato-Gastroenterology (GAEN), Institute of Experimental and Clinical Research (IREC), [2] Université catholique de Louvain (UCLouvain), Belgium, Metabolism and Nutrition Research Group (MNUT), Louvain Drug Research Institute (LDRI), [3] Université catholique de Louvain (UCLouvain), Belgium, Bioanalysis and Pharmacology of Bioactive Lipids (BPBL), Louvain Drug Research Institute (LDRI), [4] Univ. Lille, Inserm, CHU Lille, Institut Pasteur de Lille, Lille, France, U1011-EGID.

Introduction: Primary bile acids (BAs) synthesized by the hepatocytes are secreted, modified and reabsorbed in the intestine. Specifically, gut bacteria deconjugate BAs through bile salt hydrolase (BSH) activity and transform primary to secondary BAs through 7α-dehydroxylation. The deconjugation of BA is the initial gateway step of BA biotransformation in the gut and is carried out by most of the commensal bacteria of the small intestine and colon. By contrast, the transformation of unconjugated primary to secondary BAs is a multistep enzymatic pathway carried by a very small subset of anaerobic gram-negative bacterial strains. We previously showed that BAs contribute to NASH pathogenesis.

In experimental models of NASH, the enterohepatic BA pool is altered with low concentrations of secondary BAs, suggesting that bacterial BA biotransformation is impaired.
Aim: Here, our aim is to study the gut microbiota and gut bacteria BA-metabolizing activities in a NASH experimental model.
Methods: We co-housed and fed with a high fat diet (HFD) for 12 weeks foz/foz (Alms1-/-, NAFLD activity score (NAS) ≥ 6, n=8) and WT (Alms1+/+, NAS ≤ 1, n=6) mice and harvested samples after 12h fasting/4h refeeding for synchronization of BA secretion. We analyzed microbial composition of the caecal content using 16S rRNA gene sequencing, BAs by LC-MS/MS and measured BSH activity.
Results: Pertaining to gut microbiota analysis, alpha-diversity (measured by the Shannon and the observed amplicon sequence variant (ASV) indexes); and beta-diversity (reported by the Morisita Horn index) within and among caecal samples were similar in foz/foz and WT mice. The proportion of the variance explained by the genotype was low (9.2 %, p=0.32). The relative abundances of bacterial phyla and families were not significantly different, except for the Bacteroidaceae family more abundant in the caecal content of foz/foz (3.13 ± 2.10 %) than WT mice (1.27 ± 1.24 %, p=0.0076). The BSH activity in caecal content was similar in both groups, matching the similar overall microbial composition. Nevertheless, the low ratio of secondary to primary BAs and the low concentration of secondary BAs suggested a lower 7α-dehydroxylase activity in foz/foz mice. One specific ASV was detected only in 38% of the foz/foz mice while present in 100% of the WT mice at low abundance. When detected in foz/foz mice, the relative abundance of this ASV was only of 0.0056 % vs 0.0246 % in WT mice. The relative abundance of the ASV correlated significantly with the ratio of secondary to primary BAs (r=0.7786, p=0.0017), with the concentration of the secondary deoxycholic acid (r=0.8478, p=0.0006) and with the NAFLD activity score (r=-0.5891, p=0.0302). We hypothesized that this ASV identifies a small population of bacteria supporting a 7α-dehydroxylase activity, which would link its low prevalence in foz/foz mice to a low production of secondary BAs, thereby contributing to NASH pathogenesis.
Conclusions: When co-housed and fed the same HFD, the overall microbial composition is similar whether mice have NASH or not. Low concentration of secondary BAs in mice with NASH is associated to small changes in bacterial composition. Based on the ASV analysis, we identify a sequence which abundance inversely correlates with NASH. We thereby propose that discrete changes in gut microbiome with an impact on the microbial 7α-dehydroxylase activity contribute to NASH progression.

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AP-1 AND YAP1-TEAD DRIVE INDEPENDENT TRANSCRIPTIONAL PROGRAMS TO ACTIVATE HEPATIC STELLATE CELLS. V. De Smet (1), E. Van Os (1), S. Verhulst (1), I. Mannaerts (1), L. Van Grunsven (1) / [1] Vrije Universiteit Brussel (VUB), Jette, Belgium, Liver Cell Biology Research Group.

Introduction: Liver fibrosis is one of the hallmark features of chronic liver disease (CLD) and its extend is correlated with disease prognosis across aetiologies. At the cellular level, hepatic stellate cells (HSC) constitute the main source of scar tissue producing fibroblasts once they are activated from their quiescent, vitamin-A-storing, phenotype into a myofibroblast-like phenotype (aHSC). HSC activation has canonically been divided into two phases: initiation and perpetuation. We have recently shown that, at the transcriptional level, HSCs exert both initiation and perpetuation characteristics during all stages of activation and disease. As such, the relatively understudied process of initiation merits further investigation to identify HSC targeting antifibrotics in order to tackle CLD.
Aim: Identification of trans-regulatory factors involved in HSC initiation that can be used as putative targets for HSC-based antifibrotic therapy.
Methods: We reanalysed our previously published bulk RNA sequencing (RNASeq) data of initiating mouse HSCs (GSE176042). This data set consists of HSCs isolated from mice recovering from one injection of carbon tetrachloride for either 24h, 72h or 7days, where the 24h timepoint represents the initiation phase. DESeq2 was used for differential gene expression (DEG) analysis and iRegulon was used for transcriptional network prediction. Balb/C mouse HSCs were isolated using FACS-based sorting for UV positive cells and were cultured in DMEM containing 10% FBS for 10h with either a YAP1-TEAD inhibitor (Verteporfin, 1μM), an AP-1 inhibitor (T-5224, 120μM) or DMSO (control). Next, RNA was collected for RNASeq. Gene ontology (GO) analysis was performed using the Database for Annotation, Visualization and Integrated Discovery (DAVID). Gene set enrichment analysis (GSEA) was performed by using GSEA v4.1.0.
Results: DEG analysis of in vivo activated HSC RNAseq data, revealed 140 genes to be related to initiation only (24h) and 106 genes to be induced during initiation with sustained expression throughout the activation process. iRegulon analysis revealed multiple AP-1 family members to be among the top predicted transcription factors potentially regulating these gene sets. To target the AP-1 trans-regulatory function, we selected the AP-1 DNA binding inhibitor T-5224. Additionally, we selected verteporfin (VP), a YAP1-TEAD inhibitor since (i) YAP1 is a known mediator of HSC initiation and (ii) AP-1 and YAP1-TEAD have been shown to co-regulate crucial cis-regulatory elements in oncogenesis. DEG analysis of RNASeq of HSCs treated with either T-5224, VP or DMSO showed 241 and 741 genes to be differentially downregulated by T-5224 and VP respectively. These genes can thus be considered to be regulated by either AP-1 or YAP1-TEAD. Surprisingly, only 74 genes (including the known aHSC markers Col5a2 and Ankrd1) were co-regulated by both AP-1 and YAP1-TEAD. GO analysis identified distinct biological processes regulated by AP1 and YAP1-TEAD. Processes such as RNA processing and translation were attributed to AP-1 while cytoskeleton organization was attributed to YAP1-TEAD activity. GSEA revealed that both AP-1 and YAP1-TEAD significantly dysregulate the transcriptional profile of initiating HSCs by facilitating transcriptional HSC activation programs. Lastly, while T-5224 did not influence viability of culture-activated HSCs after four days, it did reduce Acta2 and Timp1 expression which indicates a reduced activation status.
Conclusions: Although AP-1 has previously been identified as a canonical mediator of HSC activation, our findings provide new insight into this trans-regulatory factor. First, while AP-1 and YAP1-TEAD have clearly been shown to physically co-operate during oncogenesis, the transcriptional landscape mediated by YAP1-TEAD and AP-1 in HSC initiation seems to be distinct. Second, we show that AP-1 mediates the earliest stages of transcriptional reprogramming of HSCs following an activating stimulus. Third, we are the first to identify that T-5224 transcriptionally blocks HSC activation. In conclusion, by analysing trans-regulatory factors implicated in HSC initiation we were able to identify T-5224 as a potential HSC targeting compound. These findings warrant further evaluation of T-5224 in relevant mouse in vivo and human in vitro models of liver fibrosis.

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REAL-LIFE MULTI-CENTER RETROSPECTIVE ANALYSIS ON NIVOLUMAB IN DIFFICULT-TO-TREAT PATIENTS WITH ADVANCED HEPATOCELLULAR CARCINOMA. N. De Wilde (1), A. Bucalau (2), G. Verset (2), L. Vonghia (3), S. Francque (3), C. Van Steenkiste (4) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Internal medicine, [2] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, [3] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Department of Gastroenterology and Hepatology, [4] AZ Maria Middelares, Ghent, Belgium, Department Gastroenterology & Hepatology.

Introduction: Hepatocellular carcinoma is a leading cause of cancer-related death worldwide. Atezolizumab plus bevacizumab has become the new standard of care for advanced HCC. Nivolumab monotherapy has proven to be effective in some cases.
Aim: This study evaluates the real-world effectiveness of nivolumab monotherapy in patients with advanced HCC, who were outside current treatment indications and reimbursement criteria for standard of care. This is a particular population of interest.
Methods: We conducted a retrospective, multicentric study, including 29 patients with HCC from 3 Belgian institutions, receiving nivolumab monotherapy after prior chemotherapy or intolerant or ineligible for the available treatment. Data were retrieved from patients' medical records. Radiological response, biological alpha-fetoprotein response, clinical response and safety profile were reported.
Results: The radiological response rate to nivolumab monotherapy was 24.1%, with a complete response rate of 13.9% and a disease control rate of 44.8%. Biological response rate was 20.7%. Radiological and biological response were strongly associated both with each other and with overall survival. Overall survival was 14.5 months (+/- 2.1), progression-free survival was 10.9 months (+/- 2.3). Seventy-eight % of patients remained clinically stable with a WHO performance status of 0 or 1 after 4 months of therapy. Grade 3 adverse events occurred in 17.2% of patients, none had grade 4 adverse events.
Conclusions: Nivolumab monotherapy is a good treatment choice in frail patients with HCC who are ineligible for standard of care or other validated systemic treatments.

- A26 -

CHRONIC LIVER DISEASE, NOT ESPECIALLY AT THE CIRRHOSIS STAGE, IS ASSOCIATED WITH INSULIN RESISTANCE AND CONFERS A RISK OF TYPE 2 DIABETES MELLITUS. G. Bale (1), F. Clarembeau (1), P. Stärkel (1), G. Dahlqvist (1), Y. Horsmans (1), N. Lanthier (1) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Service d'Hépato-Gastroentérologie.

Introduction: Insulin resistance (IR) is the precursor of type 2 diabetes mellitus (T2DM) and is defined as the inability of a given quantity of insulin to prompt a normal physiological response in insulin-sensitive tissues. Results from existing literature are clear: the prevalence of IR and T2DM is higher in patients with cirrhosis (CIR), compared to control patients (CTL) without liver disease. Some mechanisms which explain the development of IR in the context of CIR may already be present in patients with chronic liver diseases (CLD). Among these, most importantly, is liver inflammation. However, the link between non-cirrhotic CLD in general and IR is less clear-cut.
Aim: We investigate whether CIR is the primum movens of IR or if impaired insulin sensitivity is already present in non-cirrhotic patients with CLD.
Methods: Our sample population comprised three different groups: CTL, CLD and CIR. Inclusion in each of these categories was contingent on specific criteria: all patients were diagnosed following the same standards and diagnosis

was based on a blood test, transient elastography, liver ultrasound and liver histology and weren't treated for their liver disease. Metabolic dysfunction associated fatty liver disease (MAFLD) was identified in patients with steatosis and who were overweight, obese or had a metabolic syndrome as well as abnormally high liver enzymes but whose alcohol consumption was below the cut-off values for alcoholic liver disease (ALD) and where no other cause was found. Chronic hepatitis C virus (HCV) patients were diagnosed if PCR analysis yielded positive serum HCV-RNA, serology detected HCV antibodies, and augmented liver transaminases were found. For chronic hepatitis B virus (HBV), the hepatitis B surface antigen was needed along with positive RNA, HBV antibodies and increased liver enzymes. In patients not taking pharmacological treatment for T2DM, IR was quantified using the homeostasis model assessment of insulin resistance (HOMA-IR). The proportion of patients treated for T2DM was recorded in each group. Additionally, HOMA-IR levels among different disease etiologies were compared. The study was approved by the local ethics committee.
Results: 422 patients were included in our study: 16 were controls, 278 had a CLD and 128 were cirrhotic (CIR). The causes of liver disease were as follows: MAFLD (n=206), ALD (n=117), HCV (n=59), other cause (n=24). IR, represented by a HOMA-IR value exceeding 2.5, is already present in patients with non-cirrhotic CLD (median HOMA-IR 4.0). HOMA-IR levels lie between those seen in CTL (median HOMA-IR 1.3) and CIR patients (median HOMA-IR 5.7) with a statistically significant difference between the three groups (p-value <0.001). Median glycemia in the CLD and CIR groups is the same (98 mg/dL and 99 mg/dL respectively) but insulinemia is different (101.5 pmol/L and 132.3 pmol/L respectively) resulting in distinct HOMA-IR values in CLD and CIR patients (p=0.018). Compared to CLD patients, patients in the CIR group are also characterised by a higher age (51.5 vs. 62.1, p-value <0.001), lower ALT (57.7 vs. 45.6, p-value <0.001), higher AST (44.4 vs. 64.8, p-value <0.001) levels and a lower platelet count (245.4 x103 vs. 140.8 x103, p-value <0.001) consistent with portal hypertension. The number of patients with T2DM is the same in the CLD and CIR groups (36.7 and 37.5 % respectively). Finally, HOMA-IR levels differ according to disease etiology (p-value <0.001): MAFLD and HCV associated liver disease are associated with higher levels of IR (median 5.6 and 5.1 respectively) compared to ALD and other causes of CLD (median 2.9 and 3.3 respectively).
Conclusions: Chronic liver disease is associated with IR and represents a predisposing factor to the development of T2DM. Certain disease etiologies are associated with more severe IR. Cirrhosis is a factor which in itself elicits additional increase in insulin levels. This may be related to higher IR in CIR or to the portal hypertension associated with cirrhosis which results in decreased insulin clearance by the liver.

EARLY KUPFFER CELL DEPLETION DOES NOT AFFECT HEPATOCELLULAR CARCINOMA PROGRESSION IN MICE. B. Vanderborght (1), K. De Muynck (2), C. Scott (3), A. Beschin (4), M. Guilliams (5), H. Van Vlierberghe (1), L. Devisscher (2) / [1] Ghent University, Ghent, Belgium, Internal Medicine and Pediatrics (Liver Research Center Ghent; Hepatology Research Unit), [2] Ghent University, Ghent, Belgium, Basic and Applied Medical Sciences (Liver Research Center Ghent; Gut-Liver Immunopharmacology Unit), [3] VIB, Gent, Belgium, Center for Inflammation Research (Laboratory of Myeloid Cell Biology in Tissue Damage and Inflammation), [4] Vrije Universiteit Brussel (VUB), Jette, Belgium, Laboratory of Cellular and Molecular Immunology, [5] VIB, Gent, Belgium, Center for Inflammation Research (Laboratory of Myeloid Cell Biology in Tissue Homeostasis and Regeneration).

Introduction: Hepatocellular carcinoma (HCC) represents the majority of primary liver cancer cases. Its aggressive disease behaviour and poor prognosis substantiate the critical need to urgently address the lack of effective HCC treatment options. HCC usually occurs in a background of chronic liver disease (CLD), characterized by chronic hepatic inflammation and fibrosis, in which Kupffer cells (KCs), resident liver macrophages, have been proposed to play a role. However, the role of KCs in HCC initiation and progression remains unknown.
Aim: Therefore, we aim to investigate the involvement of these embryonically derived resident macrophages in the initiation of CLD-associated HCC.
Methods: For this, transgenic Clec4F-diphtheria toxin receptor mice were used. Diphteria toxin (DT)-mediated KC depletion was performed prior to the introduction of chronic liver damage in both a fibrosis-associated and a non-alcoholic steatohepatitis (NASH)-induced HCC mouse model.
Results: At the time of sacrifice, macroscopic hepatic tumours were present in approximately 100% of the cases in both HCC mouse models without differences between groups. Flow cytometric analysis of the liver tissue showed depletion of KCs and infiltration of monocytes and monocyte-derived macrophages (MoMfs), confirming previous literature, and the presence of monocyte-derived KCs (MoKCs) in both models. DT-mediated KC ablation at the initiation stage of HCC induction resulted in a decreased number of KCs and MoKCs at end-stage disease in fibrosis-associated HCC but not in the model of NASH-induced HCC. This altered hepatic macrophage pool composition was however not associated with significant changes in tumour burden, HCC markers or inflammatory, angiogenic and fibrotic components of the tumour microenvironment (TME). In NASH-induced HCC, depletion of the KCs resulted in decreased hepatic expression of alpha-smooth muscle actin and vascular endothelial growth factor, however, no differences were detected on histology for tumour burden, steatosis, inflammation and fibrosis, substantiating the limited effect of KC depletion in the initiation phase of HCC pathogenesis.
Conclusions: Despite the tolerogenic function of KCs in homeostasis and the reported role as early activators during inflammation, depletion of KCs during the initiation phase of HCC pathogenesis only has minor effects on the TME and does not affect disease severity or progression in HCC mouse models with different underlying backgrounds.

TWO DISEASES, ONE MODEL - ASSESSING THE SUITABILITY OF FOZ MICE TO EXAMINE CVD IN NAFLD. S. Bott (1), L. Dumas (2), C. Dessy (2), I. Leclercq (1) / [1] Institut de Recherche Expérimentale et Clinique (IREC), Catholic University of Louvain (UCL), Belgium, GAEN, [2] Institut de Recherche Expérimentale et Clinique (IREC), Catholic University of Louvain (UCL), Belgium, FATH.

Introduction: Non-alcoholic fatty liver disease (NAFLD) is an umbrella term which describes different states of liver disease, ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), cirrhosis and finally hepatocellular carcinoma. NAFLD case numbers are constantly rising for three decades with around one quarter of the global population being affected today. Patients with NAFLD are at higher risk of developing cardiovascular disease (CVD) - whereby most fatalities in CVD relate to atherosclerosis. Actually, CVD-dependent mortality is more frequent in patients with NAFLD in comparison to liver-related mortality. This association is related to the common metabolic risk factors such as obesity, dyslipidemia, diabetes, and hypertension shared by both NAFLD and CVD. Even more, NAFLD itself is considered as an independent risk factor for CVD (the leading cause of death globally), the link for this latter association is however still unknown. Established pre-clinical animal models only focus on one of the two diseases, yet.
Aim: The aim of this study was to assess the opportunity of using a single mouse model to examine NASH and CVD concurrently to facilitate analysis of potential mechanistic links between both diseases.
Methods: Male fat aussie mice (FOZ) and their age-matched wildtype (WT) controls were fed regular chow and high fat diet (60% kcal fat) for 24 weeks. Animals were then sacrificed, liver samples were gathered for histological assessment of the hepatic conditions, blood was sampled for determination of nitrosylated hemoglobin (HbNO) levels via electron paramagnetic resonance spectroscopy (EPR), the aorta was searched for atherosclerotic plaques and rings of first order mesenteric arteries were isolated and utilized in a wire myograph to assess carbachol (10^-8M to 10^-5M)-triggered nitric oxide (NO)-dependent relaxation to search for endothelial dysfunction, an early hallmark of atherosclerosis.
Results: FOZ mice on high fat diet (HFD) featured all hepatic characteristics of progressive NASH (steatosis, ballooning, inflammation, fibrosis; NAFLD activity score = 8), all other groups showed NAFLD activity scores below the threshold for diagnostic NASH (WT on normal diet [ND] = 0; WT on HFD = 2,8; FOZ on ND = 4,3). Although no atherosclerotic plaques were found in the aortas of FOZ mice fed a HFD, a significant reduction in their mesenteric arterial NO-dependent relaxation at a carbachol-concentration of 10^-5M compared with WT mice on HFD was detected; [$p < 0.05$]. In addition, EPR showed the lowest HbNO-level in FOZ mice fed a HFD (212,2 ± 153,2 nmol/L) whereas the remaining groups featured higher values (WT on ND: 1030,0 ± 212,0 nmol/L; WT on HFD: 288,8 ± 94,8 nmol/L; FOZ on ND: 417,1 ± 261,7 nmol/L).
Conclusions: These results demonstrate suitability of the FOZ mouse model for studies to examine CVD in NAFLD since it develops all key characteristics of progressive liver disease and endothelial dysfunction, an essential hallmark in the development of atherosclerosis which represents the main cause of death in CVD.

PREBIOTICS' PLUS PROBIOTICS' EFFECT ON THE PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE. T. Khachidze (1) / [1] Grigol Robakidze University, Tbilisi, Georgia, School of Medicine, Internal diseases department.

Introduction: Non-alcoholic fatty liver disease (NAFLD) is a very common disorder caused by a build-up of fat in the liver, often affecting overweight or obese people. Intestinal microbiota has been proved to play a role in the pathogenesis and development of obesity and NAFLD.
Aim: The aim of the study was to explore the impact of probiotics' plus prebiotics' (synbiotics) on the patients with NAFLD.
Methods: We studied 79 patients in total. Control group with placebo was included. A mixture of 6 probiotic agents (Bifidobacterium bifidum, Bifidobacterium longum, Lactobacillus fermentum, Lactobacillus plantarum, Lactobacillus acidophilus, E-Coli M-17) and an auxiliary prebiotic component: fructoligosaccharide 50 mg. was prescribed to 41 patients (I group) with elevated aminotransferase and serum triglyceride (TGs) levels for 16 weeks versus 38 patients (II group) who were given placebo. Overall, the patient's alcohol consumption accounted for less than 30g/day. Lifestyle modification was advised for both groups. Alanine aminotransferase (ALT), aspartate aminotransferase (AST), TGs, Body Mass Index (BMI), ultrasonographic grades of fatty liver were assessed in the end of the trial.
Results: Totally, 73 patients completed the study (6 dropped out in the I group). In the first group there was a significant reduction in the serum aminotransferase levels (p=0.001) and TGs levels (p=1.0) comparing the placebo group. (p=0.998

and p=0.993, respectively). BMI reduction and improvement in ultrasonographic grading was more remarkable in synbiotics' group.
Conclusions: Synbiotics showed good results in 16 weeks in the treatment of NAFLD along with lifestyle modificitanion.

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AWARENESS OF CHRONIC HEPATITIS B AND C AMONG MEN WHO HAVE SEX WITH MEN (MSM): EPIDEMIOLOGICAL SURVEY AND ON-SITE SCREENING. M. Coessens (1), T. Holvoet (2), J. Schouten (2), W. Verlinden (2) / [1] University of Antwerp, Antwerp, Belgium, Gastroenterology and hepatology, [2] AZ Nikolaas, Sint-Niklaas, Belgium, Gastroenterology and hepatology.

Introduction: In order to eradicate Hepatitis B (HBV) and Hepatitis C (HCV) by 2030, the World Health Organization focuses on screening in targeted high-risk populations, including men who have sex with men (MSM).
Aim: The objectives of the study are to assess awareness and knowledge (1) and prevalence (2) of HBV and HCV infections in the MSM population in Flanders and Brussels.
Methods: An online questionnaire in Dutch of 5 to 10 minutes was used, as well as face-to-face questionnaire using a tablet at the Belgian and Antwerp Pride (1). In 2018-2020 we joined Sensoa (a Flemish expertise center for sexual health) during outreach projects and tested visitors voluntarily at 14 gay bars, parties and saunas in Flanders by means of an oral quick test for HCV (e.g. OraSure Intercept 2). In addition, HCV test results collected by Ex Aequo (an MSM organization in Brussels that provides STD screening at offices and during on site actions) in 2019 were analyzed (2).
Results: 300 MSM participated in the online Dutch questionnaire with a median age of 36 (29.5-45) years old. HIV status was known to be positive in 7.7%. Only 73.3% and 70%, respectively, of all participants were aware that HBV and HCV are STIs. Of this group, 40.5% and 47,6% thought HBV and HCV patients would always have symptoms; 32.7% and 21,9 thought HBV and HCV have no serious complications. 21.8% thought there was no HBV vaccine; and 39.1% thought there was no medication against HBV. 52.9% thought there was an HCV vaccine; 37.1% thought there was no medication against HCV and of those who knew there was medication, 75% thought that treatment was long and hard. Only 15% and 1%, respectively, knew which sexual practices were with or without risk for HBV and HCV infection. 58.6% knew which sexual practices were risky but overestimated the risk of other practices. The degree of education was significantly correlated to the knowledge of HBV ($p < 0.001$, rs 0.209) and showed a trend towards correlation with the knowledge of HCV ($p = 0.057$, rs 0.110). The knowledge of HCV was significantly correlated to the knowledge of HBV ($p < 0.0001$, rs 0.324). The number of sexual partners in the last six months was significantly correlated to the knowledge of HCV ($p = 0.024$, rs 0.131). Sixty-six percent of all participants had performed at least one sexual practice that is known to be correlated to the risk of HCV (group sex, sharing of anal toys, sharing of anal douche, fisting and chem-sex). Though, the higher the number of risky sexual practices, the better the knowledge of HCV ($p < 0.0001$, rs 0.205). Of all participants, 62% would be interested in improving their knowledge on HBV and HCV, preferably online (82%), through a TV program (39%) or through printed material (37%). In Sensoa's HCV prevalence study, only 1 of 260 test results was positive (0.38%) and this was an HIV co-infected patient. The Ex Aequo's HCV prevalence study yielded no positive test results. The HIV prevalences were 1,15% (Sensoa) and 1,3% (Ex Aequo) and the syphilis prevalence was 2,5% (Ex Aequo).
Conclusions: There is a big knowledge gap of HBV and HCV infections in the MSM community in Flanders. To reach the WHO goals, more awareness campaigns need to be created, focussing on transmission, disease process, treatment and vaccination. These campaigns should also target people with a low educational level. The prevalence of hepatitis C infection and other STDs was low in the MSM population studied of 500 participants. Presumably a young MSM population that voluntarily has themself tested, whether or not on their own initiative, represents a rather low risk profile for HCV infection. HCV prevalence may be higher in an older population and/or in an illegal environment where more risk factors for HCV infection co-exist and that is more difficult to reach. However, given the high workload and low case finding, an on-site screening approach cannot be recommended.

BELGIAN NETWORK ON GASTROINTESTINAL REGULATORY MECHANISMS (GIREM)

- B01 -

DISTINCT MUCIN-MICROBIOME SIGNATURES IN PATIENTS WITH GASTRIC CANCER. B. Oosterlinck (1), T. Breugelmans (1), W. Arras (1), J. De Man (1), K. Geboes (2), J. Kupčinskas (3), A. Link (4), M. Peeters (5), B. De Winter (1), A. Smet (1) / [1] University of Antwerp, Antwerp, Belgium, LEMP, [2] Ghent University Hospital, Ghent, Belgium, Pathology Department, [3] Lithuanian University of Health Sciences, Kaunas, Lithuania, Department of Gastroenterology and Institute for Digestive Research, [4] Otto von Guericke University Magdeburg, Magdeburg, Germany, Department of Gastroenterology, Hepatology and Infectious Diseases, [5] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Department of Oncology.

Introduction: One of the hallmark features of gastric adenocarcinomas is aberrant mucin expression, with gastric- and intestinal-type mucins being widely expressed in gastric tumours. The clinical role of mucins in relation to disease progression and outcome is still controversial. Furthermore, the gastric microbiome is also believed to contribute to gastric carcinogenesis. Mucins can act as binding sites or metabolic substrates for bacteria and the abundance of gastric or intestinal-type mucins plays thus an important role in the site-specific colonization of bacteria in the gastric mucosa.
Aim: Here, we investigated specific mucin-microbiome signatures in patients with gastric adenocarcinomas.
Methods: Paired tumour (adenocarcinoma; stage I-IV) and adjacent normal tissue (serves as control) samples of three independent gastric cancer patient cohorts (Belgium, Ghent n=45; Belgium, Antwerp n=17; Lithuania n=43) were included. Samples were registered and stored until analysis in the Biobank Antwerpen, Antwerp, Belgium. The relative mRNA expression of gastric (i.e. MUC1; MUC5AC; MUC6) and intestinal mucins (i.e. MUC2; MUC4; MUC13) was determined by validated RT-qPCR assays. The overexpression threshold was defined as a 0.2*MNE increase (mean normal tissue expression) in the tumour compared to normal tissue. The adenocarcinomas were classified by mucin expression leading to gastric (predominantly gastric mucins), intestinal (predominantly intestinal mucins), mixed (all mucins) and null (neither gastric nor intestinal mucins) mucin phenotypes. Correlation of mucin phenotype and mucin mRNA expression with 5-year survival (Kaplan-Meijer analysis and Cox proportional-hazards model) and other clinical traits (tumour stadia, histology, age, gender, …) was also tested. The gastric microbiome was then determined using 16S rRNA gene sequencing on the Illumina platform. Quality assessment and downstream processing was performed using the DADA2 and phyloseq R packages to determine sequence taxonomy and community composition. Finally, a linear discriminant analysis effect size (LEfSe) pipeline was performed at multiple taxonomic levels to identify abundant microbial features in association with differential expressed mucins or a mucin phenotype. Finally, correlation between the microbiome and 5-year survival and other clinical traits (tumour stadia, histology, age, gender,…) was tested.
Results: Based on relative mucin mRNA expression analysis, the gastric adenocarcinomas were classified as gastric (14.5%), intestinal (25.0%), mixed (17.1%) and null (43.4%) mucin phenotypes. Furthermore, MUC13 overexpression was observed in 55.3% of the cases. Interestingly, 30% of the cohort -intestinal and mixed type- had a MUC13 expression exceeding a 1.75*MNE threshold which correlated with decreased survival ($p= 0.017$, log-rank test). Also, the 5-year survival of patients with an intestinal or null mucin phenotype was significantly ($p= 0.0078$, log-rank test) lower compared to the gastric and mixed mucin phenotypes. Microbiome composition from 43 gastric cancer patients already highlighted a lower microbial diversity based on the inverse Simpson index in the intestinal and mixed mucin phenotypes compared to the gastric mucin phenotype ($p=0.05$, Kruskal Wallis). Using the LEfSE pipeline, we were able to find 6 differentially abundant bacterial families in association with mucin phenotype groups. In the gastric mucin phenotype, the families of Leptotrichiaceae, Pseudomonadaceae and Alteromonadaceae were enriched, in the intestinal mucin phenotype the Hyphomicrobiaceae and finally the Aerococcaceae and Leuconostocaceae were enriched in the mixed phenotype. Furthermore, 5 bacterial families were found to be differentially abundant between patients with a high and low MUC13 expression. The Chitinophagaceae were enriched in the low MUC13 expressing tumours and the Flavobacteriaceae, Listeriaceae, Psychomonadaceae and Hyphomicrobiaceae were enriched in the high MUC13 expressing tumours.
Conclusions: Our results obtained so far highlight a key role for specific mucin phenotypes in predicting gastric cancer survival. Furthermore, It is also clear that an important association exists between mucins and the gastric microbiome which could influence disease progression and outcome.

- B02 -

SHORT CHAIN FATTY ACIDS AFFECT STEM CELL DIFFERENTIATION TOWARDS THE ENTERO-ENDOCRINE CELL LINEAGE IN OBESE ENTEROIDS. M. Farhadipour (1), M. Clarysse (2), K. Arnauts (3), K. Liszt (1), T. Thijs (1), L. Ceulemans (2), E. Deleus (4), B. Van Der Schueren (5), M. Lannoo (4), M. Ferrante (3), I. Depoortere (1) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing, TARGID, Gut Peptide Research Lab, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Leuven Intestinal Failure and Transplantation (LIFT) Center, [3] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing, TARGID, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium,

Department of Abdominal Surgery, [5] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Clinical and Experimental Endocrinology.

Introduction: Short-term peripheral signals regulate food intake through the release of a number of gut hormones that are secreted from entero-endocrine cells (EECs) in response to feeding and fasting cues. Obesity alters the number and content of EECs and hence their signaling to the brain. Roux-en-Y gastric bypass (RYGB) surgery is effective in inducing weight loss, which is partially due to an increase in the levels of satiety-inducing gut hormones. Prebiotic fibers that are fermented to short chain fatty acids (SCFAs) may be useful to prevent body weight gain. Studies have shown that non-digestible carbohydrates increase the number of GLP-1 containing EECs. Single-cell RNA sequencing data have provided evidence that free fatty acid receptors FFAR-2 and -3, both activated by SCFAs, are present on intestinal stem cells.
Aim: We hypothesize that targeting FFARs on stem cells or progenitor cells with SCFAs can be used to change the number of orexigenic (motilin, ghrelin) or anorexigenic (GLP-1, CCK) EECs and hence their plasma levels to mimic the beneficial effects of RYGB surgery in a non-surgical manner.
Methods: Human enteroids were generated from resection specimens from the jejunal mucosa of lean organ donors and obese patients undergoing RYGB surgery. Morphological characteristics, RT-qPCR (mucosa and enteroids), whole-mount enteroid immunostaining and radioimmunoassay were performed to evaluate enteroids as a research model. Differentiation of enteroids was initiated after 4 days of expansion. At the start of differentiation, enteroids were stimulated with SCFAs (300µM, 1mM), FFAR-2 agonist (371725, 1µM), FFAR-3 agonist (AR420626, 1µM) or vehicle. The effect of SCFAs and FFAR-agonists on stem cell differentiation towards EECs was evaluated by measuring relative gut hormone mRNA expression.
Results: Enteroids from lean individuals had a larger surface area and were characterized morphologically by more crypt developments than enteroids from obese patients during the differentiation phase. A significant correlation was observed between the relative mRNA expression of gut hormones in the mucosa and in the enteroids, indicating that the EEC signature from the primary tissue was kept in enteroids. Whole-mount enteroid immunofluorescence co-localization studies showed that gut hormones with similar functions were co-localized (e.g. motilin and ghrelin, 70% co-localization). In addition, feeding cues (e.g. peptone) inhibited, while fasting cues (e.g. norepinephrine) increased ghrelin release, indicating that enteroids were functional. Addition of SCFAs (300µM) during differentiation of stem cells reduced the relative mRNA expression of the orexigenic gut hormone ghrelin (63%, p=0.033) and tended to reduce the expression of motilin (55%, p=0.073) in obese but not in lean enteroids. No effect was observed on the mRNA expression of the anorexigenic gut hormones (GLP-1 and CCK), somatostatin and enterochromaffin-like cell marker CHGA. A higher concentration of SCFA (1mM) significantly decreased stem cell differentiation towards all gut hormones in obese enteroids. FFAR-2 and -3 agonists did not have an effect on stem cell differentiation neither in lean nor in obese enteroids.
Conclusions: Stemness differs between enteroids from lean and obese patients. Enteroids keep the EEC signature of the primary tissue, indicating that enteroids are a representative research model. SCFAs decrease stem cell differentiation towards EECs in a concentration-dependent manner in obese enteroids, but to a lesser extent in lean enteroids. The effect of SCFAs is not mediated through FFARs. We conclude that prebiotic fibers have the potential to modulate lineage commitment of intestinal stem cells.

- B03 -

EOSINOPHIL DEPLETION PARTIALLY PROTECTS FROM INTESTINAL INFLAMMATION, BUT RESULTS IN INCREASED COLLAGEN DEPOSITION IN A DSS COLITIS MODEL. I. Jacobs (1), S. Deleu (2), J. Cremer (2), J. Guedelha Sabino (2), M. Ferrante (2), S. Vermeire (2), C. Breynaert (1), B. Verstockt (2), T. Vanuytsel (2) / [1] KUL - University of Leuven, Leuven, Belgium, Microbiology, Immunology and Transplantation, [2] KUL - University of Leuven, Leuven, Belgium, Chronic Diseases and Metabolism.

Introduction: The role of eosinophils in intestinal inflammation and fibrosis in inflammatory bowel disease (IBD) is largely unknown.
Aim: Therefore, we assessed the functional role of eosinophils in a chronic murine model of colitis and associated fibrosis via anti-CCR3 mediated eosinophil depletion.
Methods: 6-8-week-old C57BL/6 RAG-/- mice received three cycles of dextran sodium sulphate (DSS) (1.75% - 2.25% - 2.25%) each interspersed with 14 days of recovery. Twice weekly, anti-CCR3 antibody (n=8), isotype (n=8) or saline injections (n=8) were given intraperitoneally. At the same timepoints, the disease activity index (DAI; mouse weight, stool consistency and presence of blood) was determined. At sacrifice, colonic damage was scored macroscopically (presence of hyperaemia, adhesions and length and degree of colon affected by inflammation). Colonic single cells were isolated and stained for flow cytometry, where eosinophils were characterized as CD45+ CD11b+ Siglec-F+ CD117- cells. Intestinal fibrosis was scored via colon weight/length, collagen deposition, using a colorimetric hydroxyproline assay and Martius Scarlet Blue staining (MSB), and COL1A1 expression by PCR.
Results: Anti-CCR3 mediated eosinophil depletion resulted in decreased disease activity compared to the other DSS treated groups injected with saline or isotype, determined by the area under the curve of the DAI (74.6±18.4 vs. 127.5±42.9 and 136.9±33.6, p=0.01 and p=0.0008 respectively). The macroscopic damage score also suggested eosinophil depleted mice to be partially protected from colonic inflammation compared to the saline and isotype injected mice that received DSS (1.1±1.0 vs. 2.1±1.2 and 3.0±0.7, p=0.09 and p=0.001 respectively). Colon weight/length and hydroxyproline assay showed a trend towards increased fibrosis in the anti-CCR3 injected group compared to saline (p=0.03 and 0.07, respectively) but not isotype (p=0.3 and 0.1, respectively) injected groups. However, COL1A1 expression levels were significantly increased in the eosinophil depleted mice compared to the saline and isotype injected mice receiving DSS (43.2±11.4 vs. 23.3±8.7 and 30.1±11.0, p=0.002 and 0.04 respectively), indicating increased collagen expression. Moreover, MSB staining showed increased collagen deposition in the anti-CCR3 treated group compared to the isotype (p=0.0008), but not the saline (p=0.09) injected group exposed to DSS.
Conclusions: Eosinophil depletion via intraperitoneal anti-CCR3 injections resulted in partial protection against colonic inflammation, but was associated with increased collagen expression and deposition. Caution is therefore needed when designing therapeutic interventions targeting eosinophils.

- B04 -

EARLY KUPFFER CELL DEPLETION DOES NOT AFFECT SCLEROSING CHOLANGITIS PROGRESSION IN MICE. K. De Muynck (1), B. Vanderborght (2), C. Scott (3), M. Guilliams (4), A. Beschin (5), X. Verhelst (2), L. Devisscher (1) / [1] Ghent University, Ghent, Belgium, Basic and Applied Medical Sciences (Liver Research Center Ghent; Gut-Liver Immunopharmacology unit), [2] Ghent University, Ghent, Belgium, Internal Medicine and Pediatrics (Liver Research Center Ghent; Hepatology Research Unit), [3] Ghent University, Ghent, Belgium, Department of Biomedical Molecular Biology (VIB Inflammation Research Center; Laboratory of Myeloid Cell Biology in Tissue Damage and Inflammation), [4] Ghent University, Ghent, Belgium, Department of Biomedical Molecular Biology (VIB Inflammation Research Center; Laboratory of Myeloid Cell Biology in Tissue Homeostasis and Regeneration), [5] Vrije Universiteit Brussel (VUB), Jette, Belgium, Cellular and Molecular Immunology (VIB Inflammation Research Center; Myeloid Cell Immunology Laboratory).

Introduction: Primary sclerosing cholangitis (PSC) is an idiopathic, immune-mediated chronic liver disease characterized by progressive sclerosis of the intra- and extrahepatic bile ducts, resulting in cholestasis, inflammation and eventually liver fibrosis. Hepatic macrophages are implicated in PSC pathophysiology, but the specific role of resident liver Kupffer cells (KCs) in the development of sclerosing cholangitis remains elusive.
Aim: To determine the effect of early KC depletion on experimental sclerosing cholangitis development.
Methods: Transgenic Clec4f-diphtheria toxin (DT) receptor mice were used to specifically deplete KCs prior to induction of disease in mouse models of intra- and extrahepatic cholestasis (3,5-Diethoxycarbonyl-1,4-Dihydrocollidine (DDC) and common bile duct ligation (CBDL), respectively). Mice were sacrificed and sampled for analyses after 3 and 2 weeks, respectively.
Results: Liver injury was successfully induced in both models and was characterized by cholestasis, inflammation, ductular reaction and fibrosis. The CBDL model showed an increased number of bile infarcts and more extensive fibrosis compared to the DDC model at study end point. Flow cytometry analysis of liver tissue of control mice showed a decreased proportion and number of KCs, with concomitant increase in monocyte-derived KCs (MoKCs) and MoMFs 3 weeks post KC depletion. In cholestatic mice, depletion of KCs and infiltration of monocytes was present in both models while the increase in monocyte-derived macrophages (MoMFs) was only present in the CBDL model despite the enhanced KC depletion in the DDC model. DT-mediated KC depletion at the initiation of sclerosing cholangitis resulted in a further decrease in proportion and number of KCs in both models, without additional impact on percentages and numbers of MoKCs and MoMFs. DT-induced KC depletion at disease induction was however not associated with significant hepatic histopathological features, including histological inflammation, ductular reaction, necrosis and fibrosis, and the expression of inflammatory and fibrosis-associated genes was also comparable in mice subjected to DDC- or CBDL-induced liver injury with and without DT-mediated KC depletion.
Conclusions: Despite the tolerogenic function of KCs in homeostasis and the reported role as early activators during inflammation, depletion of KCs during the initiation phase of sclerosing cholangitis does not affect disease progression.

- B05 -

GUT-KIDNEY CROSSTALK IN CHRONIC KIDNEY DISEASE: REMOTE SENSING OF INDOLE-DERIVED UREMIC TOXINS. M. Lauriola (1), S. Dejongh (1), R. Farré (2), K. Verbeke (2), B. Meijers (1) / [1] KUL - University of Leuven, Leuven, Belgium, Nephrology and Renal Transplantation Research Group, [2] KUL - University of Leuven, Leuven, Belgium, Translational Research in GastroIntestinal Disorders.

Introduction: The gut microbiome-host interactions are complex. Microbial metabolites are actively absorbed via intestinal drug transporters. Once they enter the systemic circulation, most of these metabolites are excreted via the

kidneys. Homeostasis is impaired in patients with chronic kidney disease (CKD), leading to accumulation of microbial metabolites often referred to as uremic toxins. Increased plasma levels of microbial metabolites are associated with, amongst others, cardiovascular events. It has been postulated that proximal tubule cells in kidneys are able to sense augmented levels of gut microbial metabolites via receptors and signaling pathways. According to the so-called remote sensing hypothesis, kidney tubular cells respond to uremic toxins plasma variations modulating the activity of membrane transporters involved in their excretion. Indoxyl sulfate (IS) and p-cresyl sulfate (PCS) originate from the microbial fermentation of tryptophan and tyrosine, two diet-derived essential amino acids. Nonetheless, few studies have investigated whether gut generation and absorption, plasma retention of microbiome-derived uremic toxins and kidney cells secretory mechanisms are affected by protein content in the diet.
Aim: We performed an animal study utilizing 5/6 nephrectomized rodent models of CKD to determine the impact of a high vs low-protein diet on indole and p-cresol absorption and on their metabolites' retention and excretion.
Methods: Eighteen Sprague-Dawley male rats (Janvier, France) 7-8 weeks old (weighing 270–388 g) were induced with CKD utilizing 5/6 nephrectomy and were randomly assigned to a low protein (n=10) or a high protein (n=8) diet. A sham-operated control group for each diet was used (n=7 and n=8 respectively). 24 hours-urine was collected after 7 weeks, and euthanasia carried out after 8 weeks from the induction of the disease. Blood and colon samples were collected. Diffusion chambers were used to assess colon permeability to indole and p-cresol over time (t=0, 60, 90, 120min). Indole concentration was quantified by Kovacs assay while p-cresol was measured with GC-MS. Creatinine was determined with standard laboratory techniques. Creatinine clearance was used as a biomarker of kidney disease severity. Plasmatic and urinary IS and PCS concentrations were measured using LC-MS/MS. The fractional excretion i.e. the percentage of uremic toxin excreted relatively to the kidney filtered load was calculated to assess remote sensing of IS and PCS.
Results: Creatinine clearance was significantly reduced (p<.001) in all 5/6 nephrectomized rats. Plasmatic IS and PCS levels were significantly higher (p<.001) in CKD rats compared to sham rats. However, CKD rats on a high protein diet showed a higher plasma level of PCS (p<.001) but no difference in plasma IS (p=0.63) compared to rats on a low protein diet. Conversely, 24-hours urinary IS and PCS were significantly increased in CKD rats on a high protein diet (p<.001). The fractional excretion of IS was significantly higher (p=0.005) in CKD rats on a high protein diet. In the high protein group, the fractional excretion of IS correlated with 24h-urinary IS (Spearman r=0.63, p=0.01) and with plasma IS (Spearman r=0.53, p=0.04). The fractional excretion of PCS did not differ among groups. These results suggest higher absorption and/or production of indole and p-cresol at intestinal level when a high protein is administered to CKD rats. Plus, they provide additional proof of the remote sensing theory of indole metabolites. The colon permeability to indole and p-cresol, evaluated ex vivo with the diffusion chamber technique, showed an increased apparent apical-to-basolateral transport of indole (p=0.049) but not p-cresol (p=0.23) in CKD rats on a high protein diet compared to that of sham rats on the same diet, again suggesting modulatory mechanisms affecting indole metabolites transporters uptake.
Conclusions: A high protein diet in 5/6 nephrectomized CKD rats leads to an increased production of indole and p-cresol in the colon and to an increased fractional excretion of IS but not PCS. These results provide an additional proof of mechanisms of remote sensing and signaling of indole-derived uremic toxins but not p-cresol metabolites. To conclude, the adoption of a low protein diet remains recommended in CKD.

- B06 -

A SINGLE-CELL SURVEY OF COLORECTAL EPITHELIAL CELLS UNVEILS MULTIPLE CELLULAR PERTURBATIONS IN PATIENTS WITH GASTROINTESTINAL DISORDERS. A. Denadai-Souza (1), Y. Wu (2), E. Modave (1), X. Abalo (3), L. Larsson (4), J. Aguilera-Lizarraga (1), S. Giacomello (3), T. Lefevre (2), K. Vandereyken (2), K. Van Beek (1), K. Bellens (1), J. Sabino (1), S. Vermeire (1), M. Ferrante (1), A. Sifrim (2), J. Lundeberg (3), T. Voet (2), G. Boeckxstaens (1) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing, [2] KUL - University of Leuven, Leuven, Belgium, Department of Human Genetics, [3] Karolinska Institutet, Karolinska University Hospital, Sweden, Science for Life Laboratory, [4] Karolinska Institutet, Karolinska University Hospital, Sweden, Science for Life Laboratory.

Introduction: The intestinal epithelium serves critical functions such as absorbing water, electrolytes and essential nutrients, while upholding a commensal microbiota and providing a barrier against invasive pathogens. Such a diverse and intricated functional repertoire is accomplished by absorptive and secretory epithelial lineages derived from common precursor cells that undergo lineage specification under the control of tightly regulated transcriptional programs. Conversely, failure of the epithelial compartment to adapt to the dynamic changes in our environment is the very core of several gastrointestinal and metabolic disorders. Therefore, a deeper understanding of both health- and disease-associated transcriptional programs at a single-cell level in the colorectal epithelium may reveal novel insights into the pathophysiology of gastrointestinal diseases such as irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD).
Aim: Herein, we designed a study aiming to build a reference transcriptional map of single colorectal epithelial cell types and states from health and diseased subjects.
Methods: In order to survey the transcriptional landscape of cells from individual subjects, we developed a new protocol for single-cell dissociation capable of capturing cell types and states at expected frequencies, down to rare populations representing less than 0.5% of the colorectal epithelium. Hence, single-epithelial cells from the rectal mucosa of health controls as well as IBS patients with predominant diarrhea (IBS-D) or constipation (IBS-C) were dissociated and subjected to single-cell RNA sequencing (scRNA-seq). Furthermore, single-epithelial cells from the colonic mucosa of non-IBD controls as well as from patients with Crohn's disease (CD) under endoscopic remission experiencing or not IBS-like symptoms were also assessed. ScRNA-seq was performed by using the Chromium Next GEM Single Cell 3' Kit v3.1 (10X Genomics). Single-cell fastqs were aligned to the human genome (GRCh38-3.1.0) using 10X Genomics Cellranger Count (6.1.2). Datasets were integrated by using HARMONY and cell types/states were annotated according to enriched gene markers. Cellular perturbations were assessed by the differential abundance analysis Milo.
Results: Our experimental strategy yielded a high-quality transcriptional landscape encompassing more than 500,000 cells, the largest single-initiative dataset of colorectal epithelial cells to this date. Our dataset unveiled stem cell heterogeneity, the transcriptional signature of three major subsets of colorectal absorptive cells as well as an in-depth transcriptional landscape of secretory cells, including progenitor and mature states of rare chemosensory cells such as tuft and enteroendocrine cells. In healthy subjects, the frequency of enteroendocrine cells was strongly enriched along with the colorectal axis. Differential abundance analysis revealed the downregulation of stem cells, tuft cells and some subsets of enteroendocrine cells, while subsets of absorptive and goblet cells were enriched in disease. Strikingly, our preliminary analysis indicated an unprecedented level of overlap in cellular perturbations between patients with IBS-D and symptomatic CD patients in remission.
Conclusions: Our dataset indicates the existence of several cellular perturbations in the colorectal epithelium of patients with IBS and symptomatic CD patients in remission. The ongoing analysis has a great potential to unravel novel cellular and molecular mechanisms underlying persistent gastrointestinal symptoms in these patient populations.

- B07 –

MUCIN MRNA ISOFORM SIGNATURES AS POTENTIAL NOVEL BIOMARKERS TO EVALUATE DISEASE STATUS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES (IBD). W. Arras (1), T. Breugelmans (1), B. Oosterlinck (1), H. De Schepper (2), M. Somers (2), E. Macken (2), F. Van Aert (2), J. De Man (1), A. Jauregui-Amezaga (2), B. De Winter (3), A. Smet (1) / [1] Laboratory of Experimental Medicine and Pediatrics, University of Antwerp, Antwerp, Belgium, Faculty of Medicine and Health Sciences, [2] Universiteit Antwerpen / Antwerp University Hospital, Wilrijk (Antwerpen), Belgium, Gastroenterology & Hepatology, [3] Universiteit Antwerpen / Antwerp University Hospital, Wilrijk (Antwerpen), Belgium, Faculty of Medicine and Health Sciences.

Introduction: Inflammatory bowel diseases, such as Crohn's disease (CD) and ulcerative colitis (UC), are characterized by perpetual chronic relapsing inflammation of the intestines. Due to their large heterogeneity, it is difficult to find the right therapy for the right patient. This demonstrates the need to find novel biomarkers to monitor IBD. Mucosal barrier dysfunction and aberrant mucin expression are major hallmarks in the pathophysiology of IBD. Furthermore, mucins are highly polymorphic, and the presence of genetic differences can alter gene expression, resulting in several mRNA isoforms via alternative splicing. While most isoforms encode similar biological functions, others alter protein function, resulting in progression towards disease. Currently, little attention has been given to the importance of mucin mRNA isoforms in IBD.
Aim: To investigate the potential of mucin mRNA isoforms as novel biomarkers for the evaluation of IBD activity and subtypes.
Methods: RNA was extracted from colonic and terminal ileal biopsies of IBD patients (both CD and UC) that underwent an endoscopy at the Antwerp University Hospital (UZA) for clinical reasons (i.e. acute flares or surveillance endoscopy when in remission). Additionally, patients without a history of IBD undergoing an endoscopy due to a positive faecal occult blood test (FOBT) which show no endoscopic abnormalities, were included as controls. Biopsies from a macroscopically inflamed (if present) and non-inflamed region from the same patient were used. The quality of the RNA samples was assessed with capillary electrophoresis and quantified using Qubit fluorometric quantitation. Library preparation was performed with the PacBio Iso-Seq multiplex protocol adapted for targeted transcriptome sequencing. Targeted capture was accomplished by using a custom-designed pool of probes, developed for the capture of MUC1, MUC2, MUC3A, MUC4, MUC5AC, MUC6, MUC7, MUC8, MUC12, MUC13, MUC15, MUC16, MUC17, MUC19, MUC20, MUC21 and MUC22 gene transcripts. Samples were sequenced on the PacBio Sequel platform at the University of Antwerp.
Results: A total of 58 samples were sequenced, comprising 47 colonic biopsies (6 control; 22 CD; 19 UC) and 11 terminal ileum biopsies. (6 control; 22 CD; 19 UC). Approximately half of all IBD samples were taken from a non-inflamed region, while the other half originates from an inflamed region. A multitude of mucin isoforms was found, of which some seem to be unique for a certain disease type (CD or UC), while others strictly occur in healthy controls. In the colon samples, a total of 8503 isoforms made it through our bio-informatics pipeline. Of these isoforms, 16.9% were shared between the IBD and control group. The largest amount of isoforms (25.9%) originated exclusively from the CD samples. 19.8% of all isoforms were only present in the UC samples and 5.9% solely occurred in healthy control

samples. In all ileal biopsies together, a total of 4689 isoforms were found. Analogous with the colon biopsies, the largest percentage of isoforms (45.3%) was exclusively found in CD patients. 5.3% and 18.3% of all isoforms only occurred in UC and control biopsies respectively. 11.4% of the isoforms were found in all patient groups of the ileal biopsies. Future efforts will be directed towards the correlation of these isoforms with disease activity and subtypes.
Conclusions: Preliminary analysis of the PacBio sequencing data indicates the presence of hundreds of novel isoforms in all patient groups and in both regions. Extensive analysis of the obtained isoform data will give more information on their clinical relevance.

- B08 -

ALTERATIONS OF THE DIFFERENTIATION AND PROLIFERATION PROGRAMS IN THE INTESTINAL EPITHELIUM COMPARTMENT CONTRIBUTE TO THE GUT BARRIER DYSFUNCTION IN ALCOHOL USE DISORDER PATIENTS. J. Lupianez (1), L. Maccioni (1), S. Ravau (1), I. Leclercq (1), P. Stärkel (1) / [1] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, IREC, Laboratory of HepatoGastroenterology.

Introduction: Chronic alcohol consumption leads to small intestinal bacterial overgrowth, changes in the duodenal mucosa-associated microbiota together with reduced immunosurveillance of microbes. The intestinal epithelium functions as a physical and chemical barrier defending the host against invading pathogenic microbes. To assure optimal homeostasis, the small intestine epithelium is constantly renewed by adult stem cells residing at the base of the crypts and by progenitor cells in the transit amplifying zone (TA). We recently showed that villi length is reduced while crypt length is increased (crypt hyperplasia) in alcohol use disorder (AUD) patients, indicating alterations in their proliferation and differentiation program.
Aim: Here, we aimed to evaluate the alterations in proliferation and differentiation in the intestinal epithelium of patients with AUD and to identify the pathways linked to these alterations.
Methods: Actively drinking patients (n=47) that were admitted to a highly standardized alcohol withdrawal program in the Cliniques universitaires Saint-Luc, Bruxelles were recruited and compared to a healthy control group (n=15) matched for age, sex and BMI. Duodenal biopsies were obtained at the second day of admission. Protein expression and tissue localisation were assessed by western blot and immunochemistry, respectively. Relative gene expression was assessed by RT-qPCR.
Results: AUD patients had significantly more ki67+ nuclei per crypt compared to control (AUD: 28.33 ±1.874 vs Ctrl: 15.93 ±3.123; p=0.002), indicating increased proliferation. Strikingly the proportion of crypt bases where adult stem cells reside showing proliferative activity was reduced in AUD (AUD: 0.78 ±0.03 Ctrl: 0.96 ±0.11; p=0.01). Increased gene expression of SOX9 and REG4, markers of progenitor cells was found in AUD patients supporting a contribution of progenitor cells located in the transit amplifying zone to the increased proliferation. The proliferative response was associated with up-regulation of target genes of the Wnt-βcatenin pathway such as Axin2, Ephb3 and CD44 indicating its activation. Protein levels of major regulators of the canonical Wnt-βcatenin pathway (GSK3β, GSK3βp and R-spondin) were not changed and consequently could not explain the increased up regulation of the target genes. Alternative pathways involved in proliferation (EGFR; Akt/mTOR and MAPK/ERK) did not show increased activation in AUD. In parallel, a higher number of goblet cells per villus and crypt was found in AUD patients compared to controls (AUD: 27.46±0.864 Ctrl: 19.03±0.055 p=0,0001), indicating a shift in differentiation towards goblet cells. KLF4 and SPDEF gene expression, transcription factors specific to goblet cell differentiation, were up-regulated in AUD. Interestingly, KLF4+ nuclei were only found in the crypts of AUD patients, further supporting a shift towards goblet cell differentiation. AUD patients showed elevated transcripts of MUC5AC, a mucin normally found in the stomach, probably related to the mucus alterations reported in those patients. Additionally, the transcript of the goblet cell related antimicrobial molecule TFF3 was increased. Those observations indicate that normal goblet cell functions might be disturbed in AUD patients.
Conclusions: Our results show an altered proliferation-differentiation program in the duodenal epithelium of AUD patients. Increased proliferation is linked to activation of Wnt-β-catenin pathway and likely originate from proliferative progenitor cells located in the transit amplifying zone. The proliferative response is accompanied by a shift towards goblet cells differentiation. In addition, altered transcripts for mucins and antimicrobial molecules indicate functional changes in goblet cells. Overall, these observations support a support a link between alterations in the epithelial proliferation/ differentiation programs and the failing gut barrier observed in AUD patients.

- B09 -

VOLATILE ORGANIC COMPOUND (VOC) PROFILING IN BREATH AND FAECAL SAMPLES DISCRIMINATES PATIENTS WITH IRRITABLE BOWEL SYNDROME FROM HEALTHY CONTROLS. K. Van Malderen (1), N. Hanning (2), H. Lambrechts (2), T. Haverhals (2), S. Van Marcke (2), J. De Man (2), B. De Winter (2), K. Lamote (2), H. De Schepper (1) / [1] Antwerp University Hospital, Edegem, Belgium, Gastroenterology, [2] University of Antwerp, Antwerp, Belgium, Laboratory of experimental medicine and paediatrics.

Introduction: Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder characterised by abdominal pain and changes in stool pattern. The Rome IV criteria are used to diagnose IBS since no diagnostic tests are currently available. Based on the dominant stool pattern patients are divided into a diarrhoea, constipation, or mixed phenotype. A promising new development to classify patients are volatile organic compounds (VOCs), which are produced by the human metabolism, inflammation, and gut microbiota, and are excreted in both faeces and breath.
Aim: The aim of this study was to evaluate the role of VOC profiling in breath and faecal samples in discriminating patients with IBS from healthy controls.
Methods: Breath samples of 72 IBS patients (27 diarrhoea, 21 constipation, 24 mixed), and 24 healthy controls (HC) were collected, as well as 81 matched faecal samples (62 IBS patients and 19 HC). Samples were analysed by multicapillary column/ion mobility spectrometry (MCC/IMS), as previously published (Van Malderen, 2020). Fresh faecal samples were snap frozen. After thawing, 0.5 grams of faeces was heated for 1 hour at 37 °C in a custom-made stainless-steel IMS-box. Headspace air and background samples were collected and analysed. The alveolar gradients of the VOCs were combined into models to discriminate IBS patients from HC, using lasso regression analysis and validated by leave-one-out-cross-validation. Models were created based on VOCs in breath, faeces, and its combination. The final models were selected based on clinical relevance with focus on specificity.
Results: Participants had a median (range) age of 27 years (18-70) for HC, 37 years (18-78) for IBS-D, 38 years (20-77) for IBS-C, and 32 years (23-64) for IBS-M patients, and respectively 54%, 85%, 76%, and 83% were female. IBS patients (overall) were differentiated from HC with a sensitivity of 72.2% in breath, 66.1% in faeces, and 71.0% in combined. Specificities were 91.7%, 78.9%, 82.4%, and accuracies were 77.1%, 69.1%, and 73.4% respectively. When comparing IBS-D versus HC we found sensitivities ranging between 63.6% and 77.3%, specificities between 70.8% and 82.4%, and accuracies between 68.3% and 79.5%. The other subtypes had lower discriminatory values with sensitivities ranging between 42.9% and 61.9%, specificities between 54.2% and 68.4%, and accuracies between 52.6% and 64.4%. Lastly, we tried to differentiate the different subtypes from each other. IBS-D could not be satisfactorily differentiated from IBS-C or IBS-M. Differentiating IBS-C from IBS-M, however, was possible with the best results in breath models with a sensitivity of 90.5%, specificity of 75.0%, and accuracy of 82.2%. Breath, faecal, and combined models all performed similarly with no significant differences in discriminatory potential.
Conclusions: Volatile organic compound profiling shows a lot of promise in differentiating IBS patients from HC. Surprisingly, the models comparing IBS patients overall with HC performed better than individual subtypes compared with HC. Furthermore, differentiating subtypes from each other was suboptimal. This could suggest that the division of patients into the classical subtypes based on stool pattern is not ideal when working with VOCs. Further research comparing patients based on other clinical characteristics, like for example disease severity, or pathophysiological mechanisms is needed to be able to optimise the use of VOCs in clinical practice.

- B10 -

THE SIX-FOOD ELIMINATION DIET IMPROVES SYMPTOMS IN FUNCTIONAL DYSPEPSIA. K. Routhiaux (1), J. Schol (2), E. Roelants (2), K. Van Den Houte (2), J. Tóth (2), I. Huang (2), F. Carbone (2), T. Vanuytsel (2), J. Tack (2) / [1] KUL - University of Leuven, Leuven, Belgium, gastroenterology, [2] KUL - University of Leuven, Leuven, Belgium, Gastroenterology.

Introduction: The Rome IV criteria define functional dyspepsia (FD) by the presence of upper gastrointestinal symptoms in the absence of readily identifiable organic abnormalities. FD is subdivided into postprandial distress syndrome (PDS), characterized by early satiation and postprandial fullness, and the epigastric pain syndrome characterized by epigastric pain or burning. Increased duodenal mucosal permeability and elevated mast cell and eosinophil counts have been reported in FD patients and was mostly associated with early satiation. Luminal food antigens are candidate triggers for these duodenal alterations.
Aim: Our aim was to evaluate the effect of the six-food elimination diet (SFED) on symptoms, gastric sensorimotor function and duodenal alterations in PDS patients.
Methods: H. pylori negative PDS patients were recruited. The SFED was followed for an 8-week period. Patients filled out the Leuven Postprandial Distress Syndrome (LPDS) diary. Duodenal biopsies were obtained before and after the diet to evaluate mucosal permeability in Ussing chambers using trans-epithelial electrical resistance (TEER) and flux of a 4KDa fluorescent-labelled dextran, and a gastric barostat study was performed. Changes in quality of life (QoL) were assessed by the Short Form Nepean Dyspepsia index. Data are reported as mean ± standard error of the mean. Results were considered significant if $p<.05$. A change in LPDS score of at least 0.7 was considered a clinically significant response.
Results: To date, 12 patients were recruited of whom 10 (8 females; 36±4years; BMI 23.03±1kg/m²) finished the SFED. PDS score improved from 1.8±0.2 to 0.9±0.3 ($p<0.0001$) resulting in a responder rate of 80%. Baseline symptoms scores for early satiation, postprandial fulness and bloating were respectively 1.6±1.0; 2.0±0.6 and 1.9±0.5, compared to respectively 0.8±0.8 ($p<.0001$); 0.9±0.9 ($p=.05$); 1.0±0.9 ($p=.05$) after 8 weeks. QoL did not significantly change (27.2±11.9 vs. 22.0±13.4; $p=.30$). Duodenal permeability including TEER (38.9±16.1 vs. 33.6±13.9 ohm.cm²) and flux (7.1±2.4 vs. 9.8±4.8 pmol) was not significantly altered (respectively $p=0.46$ and $p=0.13$). Gastric accommodation was

not significantly changed (214±47mL vs. 241±127mL, p=.92). Two patients with hypersensitivity to gastric distention at baseline normalized after the diet (p=.47).
Conclusions: This proof-of-concept study shows the potential for the SFED to improve symptoms in PDS patients, while QoL, gastric sensorimotor function and duodenal permeability are not significantly altered.

- B11 -

CENSORING REFLUX EPISODES BY THE WINGATE CONSENSUS REDUCES SUPPORTIVE EVIDENCE FOR GERD PROVIDED BY PH/IMPEDANCE MONITORING. S. Kindt (1), M. Surmont (1) / [1] UZ Brussel, Jette, Belgium, Department of Gastroenterology and Hepatology.

Introduction: The Lyon consensus classifies the evidence of gastro-oesophageal reflux (GERD) based on endoscopic features and results of pH/impedance monitoring (pH-MII). Where only an acid exposure time > 6% represents conclusive evidence for GERD, presence of more than 80 impedance episodes, low post-reflux swallow-induced peristaltic wave (PSPW) index and low mean nocturnal baseline impedance (MNBI) on pH-MII provide adjunctive evidence. The Wingate consensus established criteria to improve inter-reviewer variability when assessing reflux episodes and PSPW by impedance.
Aim: This study aims to assess the influence of the Wingate criteria on the different pH-MII parameters obtained by automated analysis.
Methods: Forty consecutive pH-MII were reviewed manually according to Wingate criteria. Number of impedance episodes censored from automatic analysis were recorded. Reflux categorisation according to Lyon consensus between censored and uncensored data was compared by Chi square. Pearson correlations between impedance parameters and censored episodes were calculated.
Results: On average 27.6 (range 3-94) impedance episodes were censored. Reasons for censoring were: 1/ anterograde episode: 13 (range 1-70), 2/ impedance drop < 50%: 4,1 (0-60), 3/ duration < 4s: 1,5 (0 – 10), 4/ <2 distal channels: 3.9 (0-20) and 5/ artefacts: 5.1 (0 – 19). Applying the Wingate criteria altered the categorisation of impedance episodes (<40 episodes, 7 vs 17 for resp. uncensored vs censored tracings, 40-80 episodes: 19 vs 19, and > 80 episodes: 14 vs 4, p=.008). MNBI and PSPW index were significantly correlated (r=.47, p=.002). The percentage of censored episodes was inversely correlated with the number of acidic impedance episodes (r=-0.61, p=0.000) and positively correlated with PSPW index (r=.64, p=.000).
Conclusions: Manual interpretation of impedance tracings based on the Wingate consensus reduces supportive evidence for GERD. The observed correlations indicate that acidic reflux episodes and reflux episodes followed by a PSPW are less likely to be censored, harbouring a potential at improving automatic pH-MII analysis.

- B12 –

RELEVANCE OF THE DIAGNOSIS OF AUTOIMMUNE GASTRITIS IN PATIENTS WITH AUTOIMMUNE THYROIDITIS. T. Haurylenka (1) / [1] Republican Research Center for Radiation Medicine and Human Ecology, Gomel, Belarus, Department of Gastrocanceroprevence.

Introduction: Autoimmune thyroiditis (AIT) occurs in 3-4% of the world's population and is 10-15 times more common in females. In the adult population, cases of AIT are recorded more often after pregnancies, childbirth, abortions, over the age of 35, in premenopausal and postmenopausal women. A family history of AIT occurs in 25-30% of cases. In the Republic of Belarus, special attention is paid to patients with thyroid pathology, which is associated with the accident at the Chernobyl nuclear power plant in 1986. The prevalence of autoimmune gastritis in the structure of gastric pathology is 10-16% according to various authors. The autoimmune component causes inflammatory-dystrophic changes in the mucous layer of the antrum and fundus of the stomach. Autoimmune gastritis is most often diagnosed in a chronic form against the background of endocrine system disorders, most of all, autoimmune thyroiditis. The genetic aspect plays an important role. There are 2 variants of autoimmune gastritis: autoimmune atrophic gastritis. With this form, hypoacid and anacid gastritis are distinguished. This situation leads to a decrease in the barrier function of the stomach, motility and a deterioration in the process of food digestion. In such a clinical scenario, the risks of developing malignant tumors and neuroendocrine tumors of the gastrointestinal tract increase. The main diagnostic method is the determination of antibodies to the parietal cells of the stomach. The second variant is chronic autoimmune gastritis. In this case, the target is the intrinsic factor –the production of specific antibodies to the protein takes place.
Aim: This protein absorbs vit B12 from food consumed, and gastromucoprotein, which creates protection for the stomach. As a variant of an unfavorable prognosis, we may observe polyfactorial and megaloblastic anemia, adenocarcinoma. Diagnostic method is determination of antibodies to parietal cells of the stomach and internal intrinsic factor. In both cases, esophagogastroduodenoscopy with multiple biopsy (OLGA / OLGIM staging system) is performed to verify the diagnosis. Early detection of autoimmune pathology of the stomach and prevention of oncological process
Methods: Taking into account the specifics of the work of the State Institution "Republican Research Center for Radiation Medicine and Human Ecology", namely the Department of Thyroid Pathology and the Center for Gastroenterological Cancer Prevention, we have developed an algorithm for the diagnosis and management of patients with autoimmune pathology. The essence of the algorithm: when autoimmune thyroiditis is detected, the patient is recommended to determine the level of pepsinogen (pepsinogen 1, 2 and ratio ½), complete blood count, biochemical blood test with mandatory determination of serum iron and ferritin levels), esophagogastroduodenoscopy (EGDS) with multiple biopsies. In the absence of anemia, according to a general blood test and a characteristic morphological picture, the patient is sent for the determination of antibodies to the parietal cells of the stomach. In the case of anemia, antibodies to parietal cells of the stomach and intrinsic factor. The ratio of the level of pepsinogens makes it possible to sufficiently judge the atrophic changes in the parietal cells of the stomach and diagnose autoimmune atrophic gastritis in a timely manner. In addition, the determination of the ratio of pepsinogens ½ allows monitoring the dynamics of atrophic changes without the use of expensive, inaccessible in most regions and traumatic tests (daily ph-impedance measurement and multiple gastric biopsy).
Results: For 2 years, together with an endocrinologist, 94 patients with autoimmune thyroiditis were examined. The study group included 11 men (average age 46 years) and 83 women (average age 39 years). In the group of men, autoimmune atrophic gastritis was established in 2 patients (18.2%). In the group of women, autoimmune atrophic gastritis was detected in 37 people (44.6%) and in 2 - autoimmune gastritis without atrophy (2.4%).
Conclusions: Thus, in a small group of patients, a preliminary conclusion can be drawn about the incidence of autoimmune gastritis in patients with AIT. In 43.6% of cases, AIT is combined with autoimmune gastritis, while significantly prevailing in females. The data obtained will be used in the future to improve the early diagnosis of autoimmune pathology of the upper gastrointestinal tract and develop recommendations for the diagnosis and treatment of such groups of patients.

- B13 -

THE PREVALENCE OF GASTROINTESTINAL SYMPTOMS DURING ACUTE COVID-19 INFECTION ASSESSED USING A DIGITAL QUESTIONNAIRE. K. Van Malderen (1), J. De Man (2), B. De Winter (2), H. De Schepper (1) / [1] Antwerp University Hospital, Edegem, Belgium, Gastroenterology, [2] University of Antwerp, Antwerp, Belgium, Laboratory of experimental medicine and paediatrics.

Introduction: COVID-19 has had a major impact on public health during the last two years. Classic symptoms like fever, cough, and loss of smell and taste are well known. Gastrointestinal symptoms, however, are often not questioned and therefore potentially underestimated.
Aim: The aim of this study was to evaluate the prevalence of gastrointestinal symptoms during COVID-19 infection.
Methods: A digital questionnaire was used to evaluate symptoms in patients suffering from COVID-19 infection. It was distributed via a patient centred informative website, COVID testing facilities, and the University of Antwerp. The questionnaire contained questions evaluating characteristics of the infection, treatment, general symptoms, and gastrointestinal symptoms.
Results: 489 questionnaires were completed, and 430 participants had a confirmed COVID-19 infection. Only data of confirmed cases was used in further analyses. Most patients (76.5%) were diagnosed with PCR testing (63% nasopharyngeal swab, 12.9% saliva, 0.6% combination of both), 7.2% were diagnosed based on serology in blood, 3.1% anamnestic by their treating physician, and 1.2% with other methods like imaging. Of our population, only 6.1% was hospitalised and 12.5% received antibiotics. Two patients (0.5%) were completely asymptomatic. The most prevalent general symptoms were fatigue (76.5%), headache (62.1%), loss of smell (60.0%), muscle aches (59.5%), loss of taste (56.7%), fever (55.6%), and cough (53.0%). All other symptoms like sore throat, rhinorrhoea, chest pain, and dyspnoea occurred in less than half of our population. A large number (82.1%) of patients had at least one gastrointestinal symptom. The most prevalent symptoms were diarrhoea and anorexia (both 52.1%) followed by abdominal pain (50.5%), nausea (40.7%), and vomiting (14.4%).
Conclusions: Individual gastrointestinal symptoms were less prevalent than most general symptoms. However, most patients in our study did have at least one gastrointestinal symptom. This demonstrates the importance of inquiring about gastrointestinal symptoms when seeing COVID-19 patients. A potential bias in our study is the possibility that patients suffering from gastrointestinal complaints are more inclined to participate in this study thereby increasing the prevalence of reported symptoms.

- B14 -

DIFFERENCES IN CALORIC INTAKE AND MACRONUTRIENT COMPOSITION IN FD AND IBS COHORTS COMPARED TO HEALTHY SUBJECTS. S. Pellens (1), K. Van Den Houte (1), F. Carbone (1), J. Tack (1) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, CROMETA.

Introduction: Functional dyspepsia (FD) and irritable bowel syndrome (IBS) are highly prevalent functional gastrointestinal (GI) disorders. It is generally accepted that in FD and IBS, symptoms can be triggered by food intake. Studies have shown that high-fat and spicy meals in particular can induce discomfort in FD. In IBS, the elimination

of fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) often results in a clear symptomatic benefit. It is unknown whether this is reflected in daily dietary intakes in these patient groups.
Aim: In this study, we aim to explore the average daily caloric intake and macronutrient composition of FD and IBS patients in comparison with healthy volunteers (HV) to gain insight into the link between diet and symptoms.
Methods: Tertiary care FD and IBS patients, currently not on a diet, were requested to complete a 4-day food diary (MyFitnessPal), including at least one weekend day. FD patients filled out the daily Leuven Postprandial Distress Scale (LPDS) diary and IBS patients the IBS severity scoring system (IBS-SSS) to record their symptoms. Additionally, we used the Rome IV questionnaire to explore GI symptoms. The overall caloric intake and proportion of each macronutrient (carbohydrates, fat and protein) were assessed and compared between patients (FD, IBS) and HV (student t-test). Furthermore, we looked for correlations between caloric intake, macronutrients and GI symptoms (Spearman correlation test).
Results: In this study, demographically similar, except for gender (p=0.03), cohorts of FD (n=26), IBS patients (n=26) and HV (n=56) participated (characteristics= FD: 81% females, 37±12 yo, 67±11kg; IBS: 79% females, 32±10 yo, 72±16kg; HV: 59% females, 41±14 yo, 69±12kg). Of all FD patients, 78% reported to suffer from postprandial fullness, 50% from early satiety and 38% from epigastric pain or burning. Pain initiated or increased in 58% of FD patients after food consumption. Bloating was commonly reported (71%), whereas belching and nausea occurred only in a minority of patients (17% and 13%, respectively). Mean LPDS (1.6±0.69) was not significantly correlated to caloric intake or macronutrients (kcal, r=-0.12; carbohydrates, r=-0.24; fat, r=-0.09, protein, r=-0.23) in patients with FD. Based on the IBS-SSS, 55% had severe IBS, 39% moderate and 6% mild IBS. There were no correlations between IBS-SSS and caloric intake, nor with macronutrients (kcal, r = -0.03; carbohydrates, r = -0.24; fat, r = -0.07; protein, r = -0.10). Compared to HV, patients ingested a smaller caloric amount (2014±505 kcal vs. FD 1792±561 kcal (p=0.02) and IBS 1752±556 kcal (p=0.04)). There was no difference in caloric intake between both patient groups (p=0.79). Looking at macronutrients, fat ingestion was shown to be significantly lower in FD compared to HV (63±27g vs. 80±25g; p=0.004), but not in IBS. Both in FD and IBS, the consumption of protein was significantly smaller in comparison with HV (67±21g vs. HV, 81±26 g; p=0.02 and 65±31g vs. 81±26g; p=0.006 respectively). Carbohydrate intakes were comparable between IBS and HV cohorts (IBS 210±67g vs. HV 224±71g; p=0.38) and between FD and HV (226 ± 76 g vs. 224±71g ; p =0.94).
Conclusions: Tertiary care FD patients have decreased caloric intake and especially avoid fat. This is in line with pathophysiological concepts and literature data. Both FD and IBS patients have a smaller caloric intake and consume less proteins, whereas carbohydrate consumption is similar to healthy volunteers. This is in disagreement with the known effects of FODMAP restriction in IBS and the uncertain role of protein as a symptom trigger in both diseases.

LACK OF EFFECT OF INTRAVENOUS CORTICOTROPIN-RELEASE HORMONE ON ANXIETY SCORES AND DUODENAL PERMEABILITY IN HEALTHY SUBJECTS. J. Luca (1), J. Schol (2), J. Tóth (2), K. Van Den Houte (2), I. Huang (2), F. Carbone (2), T. Vanuytsel (2), J. Tack (2) / [1] KUL - University of Leuven, Leuven, Belgium, Gastroenterology, [2] KUL - University of Leuven, Leuven, Belgium, Gastroenterology.

Introduction: Stress has been implicated in the pathophysiology of functional gastrointestinal disorders (FGIDs) such as functional dyspepsia and irritable bowel syndrome. The pathophysiology of FGIDs is complex and incompletely understood. However, in functional dyspepsia, increased gut permeability, low grade mucosal inflammation with eosinophils and mast cells, and altered GI sensorimotor function have been reported. Stress as well as exogenously administered corticotropin-release hormone (CRH) have been shown to increase small bowel permeability in a mast-cell dependent fashion. Moreover, eosinophil-derived CRH can activate mast cells.
Aim: The aim of the current study was to evaluate whether acute CRH administration can induce increased duodenal mucosal permeability in healthy volunteers (HVs).
Methods: Healthy volunteers without gastro-intestinal symptoms were recruited. The use of drugs such as NSAIDs, mast cell stabilizers or corticoids was prohibited. Separated by at least 1-week washout, an intravenous bolus of 100 µg CRH or placebo (NaCl 0.9%) was administered in a crossover, double blind, randomized fashion. Two hours after injection a gastroscopy with duodenal biopsies was performed. Duodenal permeability was evaluated in Ussing chambers measuring trans-epithelial electrical resistance (TEER) and the flux of a fluorescent-labeled dextran of 4kDa (FITC-D4). The State-Trait Anxiety Inventory (STAI) State version questionnaire, filled out before injection and before endoscopy, was used to estimate the participant's anxiety. In addition, during a separate baseline endoscopy, CRH was administrated ex vivo at the serosal compartment of the Ussing chambers with or without pretreatment with lodoxamide as a mast cell blocker. Results are described as mean ± SEM. P-values < 0.05 were considered significant.
Results: Eight HVs (75% women, 29 ± 2 years, BMI 24 ± 1 kg/m²) completed the protocol. No significant difference was observed after administration of placebo or CRH for TEER (30.2 ± 3.0 Ω.cm2 vs. 28.1 ± 3.2 Ω.cm²; p=0.50) or flux (respectively, 13.6 ±2.7 pmol and10.3 ±1.3 pmol; p=0.23). Anxiety scores were not altered by CRH administration (28.1 ± 1.9 at the time of placebo administration and 27.6 ± 1.7 two hours later, p=0.35; 32.0 ± 1.4 before CRH and 27.8 ± 1.9 two hours later, p= 0.14) and also did not differ between conditions at the time of injection (p=0.19) or two hours later (p=0.91). There was no correlation between anxiety scores and permeability measures. In the ex-vivo experiments, biopsies of 13 HVs (77% women, 27 ± 2 years, BMI 24 ± 1 kg/m²) could be evaluated. Compared to untreated biopsies, TEER tended to be lowered after CRH exposure (32.5± 1.3 Ω.cm² vs. 27.7 ± 2.2 Ω.cm², p=0.054). This was not prevented by co-administration of lodoxamide (27.6 ± 3.1 Ω.cm², p=0.97 compared to CRH alone, p=0.14 compared to untreated). When evaluating change in TEER from start to 90 minutes after treatment with CRH, no significant difference in change of TEER was seen between biopsies that were untreated (-7.7±0.9 Ω.cm²), pretreated with CRH (-6.2±1.5 Ω.cm²) or pretreated CRH and lodoxamide (-6.15±1.86 Ω.cm²) (p=0.09).
Conclusions: Acutely administered CRH in vivo did not induce acute anxiety and did not increase duodenal permeability in healthy subjects. However, a trend towards higher permeability was observed after ex vivo exposure of the biopsies to CRH.

- B16 -

DUODENAL INTER-CRYPTAL BUT NOT VILLOUS EOSINOPHILS ARE INCREASED IN FUNCTIONAL DYSPEPSIA AND AFFECTED BY INTER-RATER DISAGREEMENT. P. Huyghe (1), M. Ceulemans (1), G. De Hertogh (2), J. Tack (1), L. Wauters (1), T. Vanuytsel (1) / [1] KUL - University of Leuven, Leuven, Belgium, Translational Research Center for Gastrointestinal Disorders (TARGID), [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Pathology.

Introduction: Functional dyspepsia (FD) is a chronic gastroduodenal disorder with upper abdominal symptoms that remain unexplained after routine examination. With repeated findings of increased eosinophil infiltration in FD patients, focus on FD research shifted to the duodenum, proposing low-grade duodenal inflammation as a potential pathophysiological mechanism in FD (Wauters et al., Gut 2020). However, due to patchy infiltration, routine histological evaluation of duodenal eosinophils can suffer from spatial variability, potentially resulting in inter-rater disagreement and explaining contradictory findings in the literature.
Aim: We aimed to assess differences in eosinophil counts in villous versus inter-cryptal regions of duodenal biopsy sections. Additionally, we aimed to assess inter-rater reliability between different assessors.
Methods: Previously collected H&E stained duodenal (D2) biopsy sections of FD patients (Rome IV) and healthy volunteers (HVs) not taking acid suppressants were assessed. Slides were coded randomly to ensure observers were blinded to the disease status. Images were acquired with an Aperio CS2 slide scanner (Leica Biosystems, 40x magnification). Using Aperio ImageScope software (Leica Biosystems), three fields of view of both the villous and inter-cryptal region were assessed, excluding epithelial cells and crypts. The total number of eosinophils was divided by the total surface, to obtain the total amount of eosinophils per mm2. Paired t-tests were performed to compare eosinophil counts in villous and inter-cryptal regions. Additionally, unpaired t-tests were performed to compare eosinophil counts between HV and FD. The inter-cryptal regions were independently counted by a second assessor, allowing to determine the inter-rater reliability by calculating intraclass correlation coefficients (ICC) using R (v3.6.2, irr package, model = twoway, type = consistency).
Results: In total, 24 FD patients (21 female, mean ± SE age 32 ± 2 years) and 30 age- and sex-matched HVs (21 female, mean ± SE age 31 ± 2 years) were included. The mean eosinophil count (± SE) in the villous region was 95.86 ± 11.04/mm2 for HVs, and 87.27 ± 11.46/mm2 for FD patients (p = 0.60). In the inter-cryptal region, a mean of 140.43 ± 14.29 and 188.29 ± 19.41 eosinophils/mm2 was counted by the first assessor in HVs and FD patients, respectively (p = 0.05). The second assessor found a mean eosinophil count in the inter-cryptal region of 114.63 ± 8.83/mm2 for HVs and 331.07 ± 19.06/mm2 for FD patients (p < 0.001). Interestingly, eosinophil counts were significantly higher in the inter-cryptal region compared to the villous region in both HV and FD (p < 0.01). A moderate and significant inter-rater reliability (ICC = 0.443, p < 0.001) was found for the eosinophil counts in the inter-cryptal regions.
Conclusions: In functional dyspepsia, duodenal eosinophilia is only elevated in the inter-cryptal, but not the villous region of the mucosa, the latter of which showed lower eosinophil counts. In contrast to near-perfect inter-rater reliability in eosinophilic esophagitis (Vanstapel et al., Acta Gastroenterol Belg 2019), the inter-rater reliability was moderate in the duodenum. Our findings potentially explain reported differences between studies and call for uniform cell counting procedures in functional dyspepsia and eosinophilic duodenitis.

- B17 -

NEURO-IMMUNE CROSSTALK IN THE MYENTERIC PLEXUS FROM EARLY POSTNATAL DEVELOPMENT TO ADULTHOOD. M.F. Viola (1), M. Chavero Pieres (1), E. Modave (1), N. Stakenborg (1), S. Alejandro (2), K. Vandereyken (3), J. Van Herck (3), T. Martens (4), T. Voet (3), P. Vanden Berghe (4), G. Boeckxstaens (1) / [1] KUL - University of Leuven, Leuven, Belgium, Center for Neuro-immune Interaction, Translational Research Center for Gastrointestinal Disorders (TARGID), [2] KUL - University of Leuven, Leuven, Belgium, Department of Genetics, Laboratory of Multi-Omic Integrative Bioinformatics (LMIB), [3] KUL - University of Leuven, Leuven, Belgium, Department of Genetics, Laboratory of Reproductive Genomics, [4] KUL - University of Leuven, Leuven, Belgium, Laboratory for Enteric Neuroscience, Translational Research Center for Gastrointestinal Disorders (TARGID).

Introduction: The enteric nervous system (ENS) efficiently coordinates a plethora of vital functions including nutrient absorption, peristalsis and intestinal secretion. Throughout life, the gut has to significantly adapt its function to the type of food ingested, changing from milk to solid food at the time of weaning, a process that is mirrored by morphological and functional changes in the ENS. However, the mechanisms involved in ENS maturation have not been described. Macrophages are heterogeneous cells that adapt their function according to the needs of the niche in which they reside. Muscularis macrophages (MMØ) are located in close proximity to enteric neurons in the myenteric plexus during adulthood and are critical for neuronal function and survival in adulthood.
Aim: Here, we investigated the functional adaptation of MMØ to evolving tissue requirements, from early postnatal development until after weaning. Furthermore, we investigate their role in the refinement of the ENS early in life, and the role of the ENS in the establishment of a neuro-supportive MMØ phenotype in adulthood.
Methods: Neuronal (HuC/D) and synaptic (Synapsin I) density were quantified via immunohistochemistry. Pruning of synapses and neuronal phagocytosis by MMØ was analysed by quantifying engulfed synapses (Synapsin I+) and engulfed neurons using Imaris and flow cytometry respectively. MMØ were selectively depleted using anti-CSF1R at P10, P21 and 8 weeks and enteric neurons were quantified using immunohistochemistry. Cx3cr1high MMØ were sorted before, and after weaning for scRNAseq via 10X genomics. scRNAseq data was validated via immunohistochemistry and flow cytometry. Bone-marrow derived macrophages (BMDMs) were cultured for 7 days in the presence of CSF-1 and then stimulated for 24 hours with TGFβ prior to collection of cells for qRT-PCR. Enteric denervation was performed in laparotomy using 0.1% benzalkonium chloride (BAC), and tissue was collected after 5 and 14 days for RNA extraction and flow cytometry.
Results: The enteric nervous system undergoes refinement during development, with a reduction in neuronal and synaptic density from development to adulthood. This refinement is orchestrated by MMØ, that prune synapses and phagocytose neurons at significantly higher levels during development (P10) than during adulthood. Depletion of MMØ caused a significant loss of neurons in adulthood but a significant increase before weaning. scRNAseq revealed age-specific heterogeneity, with an increase in proliferating MMØ and Lyve1+ before weaning. After weaning, MMØ were predominantly undergoing terminal differentiation, or had acquired a transcriptional profile reminiscent to that of microglia (Tmem119, Hexb, Olfml3) and were closely associated to neuronal cell bodies and neuronal filaments in the muscularis externa (NA-MMØ). We observed an increase of TGFβ in the muscularis externa after weaning, and stimulation of BMDM with TGFβ was able to induce a NA-MMØ phenotype. Via flow cytometry and qRT-PCR, we determined the ENS to be a source of TGFβ in the muscularis externa. In line, enteric denervation with BAC led to a reduction in TGFβ3 expression, and the loss of NA-MMØ in the muscularis externa.
Conclusions: We identify a novel role of MMØ in refining the ENS during early postnatal development, via engulfment of synapses and enteric neurons. In adulthood, MMØ are critical for the survival of enteric neurons and adopt a neuron-associated phenotype, which is imprinted by TGFβ produced by the ENS itself. These findings demonstrate the plasticity of MMØ to adapt their function according to the environmental and developmental needs and illustrate their crucial role in ENS maintenance.

- B18 -

MRGPRB2-MEDIATED SIGNALING REPRESENTS A NOVEL MAST CELL DEGRANULATION PATHWAY IN THE MOUSE COLON. S. Van Remoortel (1), L. Lambeets (1), J. De Man (2), B. De Winter (2), S. Ibiza Martinez (1), J. Timmermans (1) / [1] University of Antwerp, Antwerp, Belgium, Veterinary Sciences, [2] University of Antwerp, Antwerp, Belgium, Translational Research in Immunology and Inflammation.

Introduction: It has been known for decades that mast cells, in addition to canonical IgE-FcεRI crosslinking, also are directly activated, in an IgE-independent manner, by a number of distinct cationic substances such as antimicrobial peptides and inflammatory (neuro)peptides. However, only recently were the exact receptor signaling mechanisms contributing to this IgE-independent activation identified. More specifically members of the Mas-related G protein-coupled receptor (Mrgpr) family, i.e. Mrgprb2 in mice and its human counterpart MRGPRX2 were found to be crucial players in these pathways. Since their discovery, Mrgprb2/MRGPRX2 have redefined the classic concept of mast cell activation and have emerged as a distinct pathway driving immediate drug hypersensitivity, chronic itch conditions, antibacterial immunity and neurogenic inflammation and pain. Remarkably, whereas most studies have focused on the role of Mrgprb2/MRGPRX2 in skin mast cells, little is known on the relevance of this pathway in mast cells residing in the gut.
Aim: To assess the relevance of Mrgprb2-mediated signaling in the healthy and diseased mouse colon.
Methods: A genetic labeling strategy was used to identify and characterize the presence of Mrgprb2-expressing mast cells in the healthy and diseased colon. Furthermore, Mrgprb2 receptor knockout mice were used to elucidate the functional role of Mrgprb2 receptor signaling in mast cells of the healthy and diseased colon.
Results: In the colon of healthy Mrgprb2-cre:tdTomato mice, we observed tdTomato+ cells that co-labeled with established mast cell markers. These Mrgprb2-expressing mast cells were mainly located in the lamina propria and submucosa, where they resided in close proximity to neuronal fibers. Furthermore, ex-vivo exposure to known Mrgprb2 ligands induced mast cell degranulation and mediator release. These Mrgprb2-expressing mast cells were markedly increased in the DSS-induced acutely inflamed colon, as evidenced by an increased Mrgprb2 mRNA expression and concomitant increases in Mrgprb2-expressing mast cells.
Conclusions: Our findings support the relevance of Mrgprb2-mediated signaling in colonic mast cells, thereby warranting further studies into the role of this IgE-independent pathway in inflammatory and functional gut disorders.

- B19 -

MICRORNA PROFILING OF ENTERIC GLIA STATUS. A. Holland (1), A. Bon-Frauches (2), F. Progatzky (3), D. Keszthelyi (4), D. Jonkers (4), V. Pachnis (3), V. Melotte (2), W. Boesmans (1) / [1] Hasselt University, Hasselt, Belgium, Biomedical Research Institute (BIOMED), [2] Maastricht University Medical Center, The Netherlands, Department of Pathology, GROW-School for Oncology and Developmental Biology, [3] The Francis Crick Institute, United Kingdom, Development and Homeostasis of the Nervous System Laboratory, [4] Maastricht University Medical Center, The Netherlands, Department of Internal Medicine, Division of Gastroenterology-Hepatology, NUTRIM-School of Nutrition and Translational Research in Metabolism.

Introduction: Enteric glial cells (EGCs) constitute a heterogeneous and highly plastic population of peripheral neuroglial cells embedded in the gastrointestinal tract. They are integral players in the maintenance of intestinal homeostasis and their activity also profoundly influences gut pathophysiology; yet, the molecular underpinnings that govern EGC status are incompletely understood. MicroRNA-mediated gene regulation is critical for 'tuning' cellular dynamics in many organ systems and diseases. However, to date, specific microRNA profiles have not been assigned to EGCs, and the role of microRNAs in EGC phenotype and function are unknown.
Aim: Ergo, our primary purpose is to elucidate the role of microRNA-mediated regulation of EGC identity and activity during gastrointestinal homeostasis and disease.
Methods: To identify microRNAs expressed by EGCs we performed microRNA sequencing of FACS-sorted EGCs isolated from Sox10-CreERT2;nuclGFP mice. This was combined with a targeted approach based on 1) evolutionary conservation, 2) differential expression in gastrointestinal disorders, and 3) ability to tune dynamics of CNS glia. The expression of microRNA candidates in healthy human colonic biopsies and murine colonic and small intestinal tissues was examined using qPCR. MicroRNA expression in EGCs was confirmed using fluorescence in situ hybridization (miRNAscope), and their dynamics were evaluated in both in vitro and in vivo models of enteric gliosis.
Results: Several microRNAs were found to be expressed in the sigmoid colon of healthy volunteers and in the mouse colon and small intestine, albeit differentially, with the highest microRNA levels detected in the colon. Specific microRNAs were also detected in isolated murine myenteric plexus preparations of the colon and small intestine, with the highest transcript quantities detected in the distal colon and duodenum. Expression of a selection of microRNAs was confirmed in both primary and secondary EGC cultures and a robust time-dependent increase of miR-146 levels was observed in reactive EGCs.
Conclusions: This is the first evidence for microRNA expression in EGCs. Our results allude to regional microRNA expression specificity, reveal distinct microRNA signatures that can mark EGC identity, and suggest a possible role for miR-146 in establishing the 'reactive' status of EGCs.

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GLIADIN CYTOTOXICITY ON ENTERIC GLIAL CELLS: NOVEL INSIGHTS ON CELIAC PATHOGENESIS BASED ON A NEW ENTERIC GLIAL CELLS IN VITRO MODEL. L. Zanoletti (1), A. Valdata (2), K. Nehlsen (3), P. Faris (2), C. Casali (2), R. Cacciatore (4), I. Sbarsi (4), F. Milella (2), F. Carriero (2), C. Martinelli (2), G. Barbieri (2), L. Van Baarle (1), V. De Simone (1), E. Raimondi (2), T. May (3), F. Moccia (2), G. Matteoli (1), S. Comincini (2), F. Manai (2) / [1] KUL - University of Leuven, Leuven, Belgium, TARGID, [2] University of Pavia, Pavia, Italy, Department of Biology and Biotechnology "L. Spallanzani", [3] InScreenEx GmbH, Braunschweig, Germany, InScreenEx GmbH, [4] IRCCS Policlinico San Matteo, Pavia, Italy, Immunohematology and Transfusion Service.

Introduction: Celiac disease (CD) is a chronic immune-mediated disease belonging to the gluten-related disorders which affects the small intestine of individuals with genetic predisposition. The main histopathological marker is villous atrophy, a condition associated with malabsorption. Nowadays, the only available treatment for celiac disease is gluten free diet (GFD), which leads to complete recovery of villous atrophy and resolution of antibody response after few months. In the last decades, several studies suggested enteric glia as a key player in intestinal immunity and inflammation in both physiological and pathological conditions. It is now clear that enteric glial cells (EGCs) contribute to the maintenance of epithelial barrier integrity and to the protection against bacterial infections. On the other hand, EGCs have been reported to trigger and support bowel inflammation in pathological conditions, such as inflammatory bowel diseases (IBDs). Considering that CD shares mutual features with IBDs, it is reasonable to hypothesize that EGCs also influence the onset and the development of CD. Despite this fact, to date there are few data regarding the involvement of EGCs in CD pathogenesis.

Aim: The current study aimed to investigate the effects of enzymatically digested gliadin, the cytotoxic component of gluten, on a new in vitro model of human EGCs generated through lentiviral transduction.
Methods: Human EGCs were derived from the colon of a 75-year-old female donor and immortalized through a lentiviral transduction protocol (Lipps et al., 2018). The obtained cells were then characterized for the expression of the specific EGC markers (i.e. GFAP, S100β, Sox10) and their cumulative population doubling level (cPDL) was calculated and compared to that of post-isolated primary EGCs. These cells were also characterized from a cytogenetic and physiological point of view through metaphase spreads preparations and Ca2+signals measurements with Fura-2. Subsequently, peptic-tryptic digested gliadin (PT-gliadin) was administered to EGCs and different analyses were performed to evaluate cell viability, oxidative stress level, mitochondrial depolarization, and apoptosis through different techniques, such as MTS, immunofluorescence (IF), transmission electron microscopy, cytofluorimetric and immunoblotting assays.
Results: The isolated hEGCs showed a cPDL higher to that of primary EGCs whereas morphological analysis revealed no differences. Real-Time PCR and IF demonstrated the expression of the specific EGC markers. Furthermore, the consensus karyotype was identified as well as the Ca2+ signalling response to well-known glial neurotransmitters (i.e. ATP, acetylcholine, serotonin and glutamate). The effects of PT-gliadin to EGCs were evaluated firstly through MTS assay and brightfield microscopy. Both analyses showed that cell viability significantly decreased at 12 and 24 hours p.t. following 0.5 µg/uL and 1 µg/uL of PT-gliadin administration compared with non-treated (NT) cells. Considering that α-gliadin peptides intake, in particular p31-43, induces oxidative stress and the intracellular increase of reactive oxygen (ROS) and nitrogen (NOS) species, intracellular ROS levels were then measured at 3 and 6 hours p.t. through cytofluorimetric analysis. As a result, statistically significant increase in ROS levels was observed at both treatments with a concentration-dependent trend. Mitochondria are one of the main targets of ROS exposure. Particularly, high levels of ROS associated with oxidative mtDNA damage play a major role in apoptosis. Considering these premises, mitochondrial health and apoptosis induction were analysed after the administration of PT- gliadin through cytofluorimetric assay, immunoblotting, fluorescence and electron microscopy evaluations. Results suggested that gliadin was able to induce severe morphological alterations as well as a decrease in mitochondrial transmembrane potential (ΔΨm), thus leading to impaired mitochondrial function. The observed mitochondrial damage agreed with the increase of effector caspases (i.e. caspase-3 and caspase-7), suggesting that apoptosis is the elected death pathway of EGCs after PT-gliadin administration.
Conclusions: These preliminary data showed the cytotoxic effects of gliadin towards EGCs. Particularly, the administration of PT-gliadin led to an increase in ROS intracellular levels and mitochondrial damage, thus resulting in cell death mediated by the apoptotic pathway. Consequently, these results might suggest the involvement of enteric glia in CD pathogenesis References Lipps C, Klein F, Wahlicht T, et al. Expansion of functional personalized cells with specific transgene combinations. Nat Commun. 2018;9(1):994.

LIVE IMAGING OF PRIMARY NEURONS IN LONG-TERM CRYOPRESERVED HUMAN NERVE TISSUE. M. Fortea (1), P. Jain (2), I. Demedts (3), J. Tack (4), T. Vanuytsel (4), C. Cirillo (5), P. Vanden Berghe (1) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), Lab for Enteric Neuroscience (LENS), KU Leuven, Leuven, Belgium, LENS, [2] Translational Research Center for Gastrointestinal Disorders (TARGID), Lab for Enteric Neuroscience (LENS), KU Leuven, Leuven, Belgium, LENS , [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Chronic Diseases and Metabolism (TARDGID) and Department of Gastroenterology and Hepatology, [5] Tolouse NeuroImaging Center, Inserm, University Paul Sabatier, France, ToNIC.

Introduction: Tissue cryopreservation provides a convenient solution for tackling one of the major problems in neuroscience research, namely the scarce availability of human nerve tissues, especially if needed alive. While brain tissue can be used only post-mortem, live nerve tissue can reasonably well be harvested from the periphery. A valuable source of primary neurons is the intestine, which compared to brain has the advantage to be safely accessible via endoscopy. The nerve tissue innervating the intestine (the enteric nervous system) can be sampled with regular endoscopic biopsy forceps and remains viable for multiple physiological and immunohistochemical tests, as previously demonstrated. Moreover, also functional assays were proven possible. A series of studies have now demonstrated the value of the submucosal plexus obtained from intestinal biopsies, which, in combination with live microscopic imaging, can be used to assess human neuron and glial cell function.
Aim: To expand the applicability of human submucous neurons for live microscopic imaging by establishing a viable long time cryopreservation protocol.
Methods: Colonic mucosal biopsies were collected and either directly cryopreserved or dissected to obtain the submucosal plexus. Different protocols for tissue cryopreservation were tested, considering different temperatures and freezing agents like DMSO and isopentane. These cryopreserved primary neurons were evaluated for morphology (histology) and functionality (live imaging and cell responsiveness to high K+, 5HT and DMPP) after cryopreservation of up to one-year. Histology evaluation was performed under the following conditions: (1) Directly fixed tissue; (2) Fixed after 1 week of cryopreservation without DMSO [W1w/oD]; and (3) Fixed after 1 week of cryopreservation with DMSO [W1wD]. Live imaging was performed at different cryopreservation timepoints and conditions: (1) Freshly isolated SMP [FI], (2); 1 day cryopreserved without DMSO [D1w/oD]; (3) 1 day cryopreserved with DMSO [D1wD]; (4) 1 week cryopreserved with DMSO [W1wD]; (5) 3 months cryopreserved with DMSO [M3wD] and (6) 1 year cryopreserved with DMSO [Y1wD]
Results: The use of the cryoprotective agent DMSO and the application of isopentane for controlled cooling revealed to be crucial to properly store the nerve tissue and to enable functional measurements after thawing. Hematoxilyn & eosin stainings showed an intact architecture in each of the conditions tested. NSE and S100 staining showed no changes in terms of cellular integrity of enteric neurons or glia when comparing the three groups (freshly fixed or one week cryopreservation with or without DMSO). Therefore, we can assume that the cryopreservation process does not alter either the histology of the tissue or the presence of enteric neurons or glia. HuCD immunofluorescence staining did not reveal any difference in the number of ganglia per biopsy among groups nor in the number of neurons per ganglia. Yet, nuclear HuCD staining, indicative of poor neuronal health, was increased in tissue preserved without DMSO (D1w/oD) when compared to FI and tissue preserved with DMSO (D1wD). Calcium imaging was used to test whether human primary neurons remained viable and responded to high K depolarization. The percentage of responding ganglia in tissues preserved without DMSO (D1w/oD: 5.3 (11.8) %) was substantially lower than in FI tissues (FI: 90.5 (11.1) %) or those cryopreserved in the presence of DMSO (D1wD: 88 (18.2) %, (NS), W1wD:100 (16.7) % (p-value: 0.004) and M3wD: 100 (0) % (p-value: 0.02) and Y1wD: 100 (6.1) %). No differences were found between FI SMP neurons response and those preserved with DMSO, independently of the cryopreservation period ($p>0.05$). Additionally, cryopreserved human ENS is able to respond to selective stimulations as well, including serotonin and nicotinic receptor activation after 1 week, 3 months or 1 year of cryopreservation.
Conclusions: The human enteric nervous system is a realistic source of primary neurons, which can be successfully preserved over long times and as such can be exploited both for gastrointestinal specific as well as for general neuroscience research. This protocol also favors the expansion of research networks, broadening collaborations among institutes with different expertise, by providing a unique tool to those research institutes not associated with hospital centers.

STUDY OF NEURODEGENERATION AND GASTROINTESTINAL MOTILITY DURING DIET-INDUCED OBESITY. M. Chavero Pieres (1), M. Viola (1), G. Boeckxstaens (1) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Chronic diseases, Metabolism and Ageing.

Introduction: Obesity has reached epidemic proportions worldwide, placing a huge health and economic burden on society. Obese patients suffer from cardiovascular diseases, metabolic disorders and gastrointestinal complaints, including constipation. Several studies have suggested that constipation or delayed gastrointestinal transit in preclinical models of obesity results from high fat diet (HFD)-induced gliosis and loss of enteric neurons. Of note, however, these studies used high-fat purified diets, which amongst other characteristics, contain reduced amounts of fiber compared to the commonly used non-purified diets for rodents. As differences in dietary fiber content largely impact on gut physiology and alter the composition of the microbiome, the outcome of these studies may be significantly biased.
Aim: We evaluated the effect of purified HFD-induced obesity on enteric neurodegeneration and gastrointestinal transit compared to a purified control diet.
Methods: Male C57/BL6J mice were fed a purified HFD or purified control diet for up to 12 weeks. Mice were fasted overnight prior to assessment of whole gut intestinal transit time (WGTT) via carmine red gavage. Faecal output was assessed for the duration of 2 hours. Food consumption was measured by weighing the food prior starting and after the transit assessment. Assessment of the effect of food intake on WGTT was performed in male C57/BL6J mice of 12 weeks old with either restricted (0.2g) or ad libitum access to normal chow diet. Colonic muscularis externa was collected for immuno-histochemical staining (IHC) and confocal imaging of enteric neurons. Images were analyzed using ImageJ (Fiji) software.
Results: 12 weeks after treatment, neuronal density in the distal colon muscularis externa was unchanged in the HFD-treated mice (566±85 neurons/mm2) compared to controls (622±90 neurons/mm2; $p=0.17$; $n=10$). Both low fat and high fat purified diet induced an increase in WGTT after 2 weeks of feeding (96±11 min and 87±7 min before diet and 187±40 min and 149±28 min 2 weeks after diet onset in the HFD and control groups, respectively; $p=<0.0001$; $n=9$-10). WGTT was significantly increased in the HFD-treated group from week 4 (255±58 min) compared to the controls (152±26 min; $p=0.02$; $n=9$-10) and the delay became even more pronounced in the HFD group at later timepoints (532±81 min) compared to the controls (178±66 min; $p= <0.0001$; $n=9$-10). Mice receiving HFD displayed reduced food intake during WGTT assessment (0.7±0.4 g) compared to controls (2.0±0.2 g; $p=<0.0001$; $n=8$-10). Reduced food intake in non-obese control mice induces a delay in transit (374±54 min) compared to mice fed ad libitum (165±37 min; $p=<0.0001$; $n=7$). Faecal output remained unchanged throughout the course of the experiment between the HFD (0.09±0.04 g/2h at 12 weeks) and control mice (0.09±0.03 g/2h at 12 weeks; $n=9$-10).
Conclusions: HFD-induced obesity did not induce neurodegeneration in the colonic muscularis externa. Purified diets are sufficient to induce an increase in WGTT regardless of fat content. We identified differences in food intake as an experimental bias in the WGTT assessment. A constipation-like phenotype could not be detected when faecal output was assessed. These findings highlight the importance of selecting appropriate control diets in studies on gastrointestinal physiology and raise further questions about the impact of purified diets as a confounding factor.

CASE REPORTS

- C01 -

LARGE SUPERFICIAL SQUAMOUS CELL CARCINOMA IN THE SETTING OF ACHALASIA TREATED BY ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD): PARTICULAR FEATURES OF SUPERFICIAL CARCINOMA ON STASIS RELATED ESOPHAGEAL HYPERKERATOSIS. L. Mesureur (1), R. Yared (1), L. Verset (2), J. Van Laethem (1), H. Louis (1), J. Devière (1), A. Lemmers (1) / [1] Erasme Hospital, Brussels, Belgium, Gastroenterology Department, [2] Institut Jules Bordet, Brussels, Belgium, Pathology Department.

Case Report: A 69-year-old man presented with solid food dysphagia and weight loss since few years was referred after the discovery of a 6mm lesion at 30cm from incisors with high grade dysplasia. Computed tomography demonstrated stasis of the distal esophagus and esophageal wall thickening. High resolution manometry disclosed absent esophageal peristalsis but lower esophageal sphincter acceptable relaxation. High resolution endoscopy revealed in the lower two thirds of the esophagus a keratinized mucosa. A surprising large flat (O-IIb) suspicious squamous dysplastic lesion was observed on 50% circumference from 30 to 40cm of the incisors. Narrow banding imaging and near focus revealed Type B2 intrapapillary capillary loops. Lugol chromoendoscopy confirmed the delineation of the lesion and its suspicious feature. En-bloc endoscopic resection using ESD was performed from 29 to 40 cm of the incisors up to 60% of the circumference. Stricture prevention modality within loco triamcinolone injection was offered associated with proton pump inhibitors treatment. The histopathological analysis of the 118x95mm specimen revealed a squamous cell carcinoma (SCC) in situ of 100mm with a focal 9mm site of malignancy (pT1am3 moderately differentiated squamous cell carcinoma without lymphovascular, perineural invasion or tumor budding). Deep and lateral margins were free. The resection was curative. Endoscopic follow-up was proposed with control at 3, 6 and 12 months, with complete healing of the ESD scar without stricture or signs of recurrence. Symptoms of dysphagia resolved in the meanwhile as well as weight loss. Due to the difficult of detection of esophageal SCC in hyperkeratinized esophagus, superficial carcinoma is reported in only 9.1% of the cases. The particularity of this case is the feature of large superficial SCC in the setting of stasis and keratinized esophagus associated to achalasia.

- C02 -

GASTRIC PERORAL ENDOSCOPIC MYOTOMY (G-POEM) FOR REFRACTORY POSTSURGICAL GASTROPARESIS. P. Casteels (1), M. Aerts (1), R. Kunda (1), S. Kindt (1) / [1] UZ Brussel, Jette, Belgium, Gastroenterology.

Case Report: We present a 63-year-old patient with severe regurgitation and nocturnal coughing following gastric pull-up surgery for esophageal cancer 12 years earlier (2009). During oncological follow-up, gastric retention was repetitively documented by endoscopy and medical imaging. Disabling symptoms persisted despite pyloric dilation, laparoscopic pyloroplasty, botulin toxin injection and various attempts at medical therapy (antacids, high dose PPI, prokinetics, somatostatin analogues, prucalopride). Eventually, G-POEM was performed in 2021. The procedure was uneventful. At follow-up, the severity of gastroparesis, assessed by the gastroparesis cardinal symptoms index, improved significantly, with no apparent side effects. Discussion: Postsurgical gastroparesis following foregut surgery, is a chronic motility disorder which can prove challenging to treat, with an estimated incidence of 0.4% to 5%. It is defined by symptoms of delayed gastric emptying without evidence of mechanical obstruction. When other treatment options fail, gastric peroral endoscopic myotomy (G-POEM) has been proposed. G-POEM is a minimally invasive endoscopic technique in which a pyloric myotomy is performed through construction of a submucosal tunnel. Multiple case reports confirm the safety and clinical effectiveness of G-POEM for postsurgical gastroparesis. Controlled studies comparing G-POEM to other approaches are lacking. To our knowledge, this is the first case report on the value of G-POEM for persisting gastroparesis symptoms despite prior pyloroplasty.

- C03 -

AN UNUSUAL LOCATION OF ABDOMINAL GAS. P. Corens (1), J. Derdeyn (2), I. Baar (3), L. Vonghia (2), T. Steinhauser (2), T. Vanwolleghem (2), S. Francque (2), W. Kwanten (2) / [1] Universiteit Antwerpen / Antwerp University Hospital, Wilrijk (Antwerpen), Belgium, Gastro-enterology, [2] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastro-enterology and Hepatology, [3] Antwerp University Hospital, Edegem, Belgium, Intensive Care.

Case Report: Herein we report the case of a rare ultrasound finding. A 29-year-old patient who was diagnosed with acute lymphoblastic leukemia complicated with hyperviscosity syndrome and marked hyperleukocytosis was admitted to the Intensive Care Unit where cytoreductive therapy and leukapheresis was initiated. In the consecutive days the patient developed respiratory deterioration due to progressive pleural effusion requiring intubation and mechanical ventilation. Simultaneously autologous stem cell transplantation was performed. During further hospitalisation, the patient developed a catheter-related bloodstream infection with Enterococcus faecium requiring removal of a jugular vein catheter and placement of a new venous access in the left femoral vein. Following the occurrence of thrombopaenia [21 x 10E9/L] and a progressive increase of liver enzymes [ASAT 565 U/L, ALAT 856 U/L, AP 368 U/L, GGT 976 U/L] and direct bilirubin [11 mg/dL], an abdominal ultrasound was performed to evaluate the liver and the likelihood of hepatic sinusoidal obstruction syndrome (SOS) in particular. Hepatosplenomegaly in the absence of structural abnormalities at the liver parenchyma or bile duct system was seen. Furthermore, a thickened gallbladder wall (8.5 mm) with the presence of cholecystolithiasis was found in addition to mild ascites. Evaluation of the liver vasculature revealed hyperechogenic flat reflectors with acoustic shadowing and reverberation artefacts (comet tails) in the mid- and left hepatic vein suggestive of venous gas. These findings were not present in the inferior vena cava, right atrium, portal vein and there were neither signs of aerobilia. Subsequent evaluation with duplex-mode revealed normal flow signals of the liver vasculature. Additional investigation with CT-abdomen with intravenous contrast several days later revealed no abnormalities at the liver parenchyma except for focal steatosis in segment IV and VII, no intra-abdominal inflammatory processes were present. At the level of side branches of the hepatic vein, two hypodense foci could be noted, presumably consistent with the presence of gas correlating with previous ultrasound findings, although less pronounced. Abdominal ultrasound 7 days after initial ultrasonographic evaluation showed complete resolution of previously detected hepatic gas. Initial findings could point to possible SOS, according to clinical and ultrasound criteria, albeit there was no increase in portal venous diameter or reversal of its flow on duplex. Due to the patient's poor clinical condition and possible procedure-related complications (air embola), we refrained from an additional transjugular liver biopsy. In the following days, a spontaneous trend towards normalization of the altered liver enzymes and direct bilirubin, arguing against SOS, was observed. Unfortunately, in spite of hepatic improvement, patient deceased due to multiple organ failure. The presence of portal venous gas is a recognised finding in patients with intestinal ischemia or intra-abdominal sepsis with poor outcome. On the contrary, air in the hepatic veins is less frequently encountered. In literature, only a few cases are described of patients diagnosed with hepatic venous gas as a consequence of either abdominal trauma, pyogenic liver abscess with Klebsiella pneumoniae or previous catheterisation of the femoral vein. Isolated cases are reported of synchronous portal and systemic venous air in patients with intra-abdominal infection who were afterwards diagnosed with a patent ductus venosus or portosystemic fistula. In this patient, we assume the diagnosis of hepatic venous gas as a consequence of prior placement of a central catheter in the femoral vein. Other possible causes such as abdominal inflammatory processes or bacteriaemia with gas-forming bacteria were excluded, whereas the hepatic venous air spontaneously resolved. Placing a catheter in the femoral vein might act as a possible entrance port for gas in the systemic venous system that entered the hepatic veins in a retrograde manner. Considering anatomy of the venous system, this finding presumably does not occur after subclavian or jugular central venous catheterization. While portal venous gas is associated with serious underlying conditions, hepatic venous gas could be an incidental and when limited presumably innocent finding following the placement of a femoral vein catheter as described in this case.

- C04 -

INFECTIOUS DISEASE MIMICKING A METASTATIC RECTAL CANCER. N. El Nakadi (1), L. Mans (2), A. Buggenhout (1), N. Bachir (1) / [1] Erasme Hospital, Brussels, Belgium, Colorectal Surgery, [2] Erasme Hospital, Brussels, Belgium, Gastroenterology.

Case Report: We report the case of a 47-y-old man, presenting with lumbar pain, 39°C Fever, diarrhoea, nocturnal sweating and 4 kg weight loss in the last 3 weeks. He came to our institution with the diagnosis of metastatic lower rectal tumour based on an abdominal CT-scan. The complementary assessment by pelvic MRI, total body Pet-FDG and thoraco-abdominal CT-scan demonstrated: a hyper-metabolic left lower rectal tumour with thoracic, retroperitoneal splenic and mesorectal adenopathies (T3c MRF + EMVI – N2). The Pet-FDG suspected a hyper-metabolic hepatic metastasis in the VI segment. The total colonoscopy and echo-endoscopy confirmed a non-obstructive sub mucosal tumour of the lower rectum/anus (20x45x15mm), invading the internal anal sphincter. (uT2-4Nx). The histological analysis of the superficial biopsy was normal with no malignancy or pathogen. Blood analysis showed high CRP level (84,3 mg/L). CEA and CA 19-9 were normal. Blood and urinary cultures were negative. A surgical trans-rectal true-cut biopsy was performed under general anaesthesia. No dysplasia or malignancy was found on histological analysis. A complementary hepatic MRI showed two suspicious hepatic lesions in segment V and VIII. Without any histological evidence of malignancy, we decided to perform a hepatic biopsy and a surgical biopsy of 3 right inguinal hyper-metabolic lymph nodes. The histological analysis concluded in normal hepatic parenchyma and only one of the 3 lymph nodes presented focal necrotic granuloma without any sign of malignancy. After one month of investigation and no histological evidence of malignancy, the patient presented no more temperature and a normal CRP but continued having nocturnal sweating and weight loss (8kg, 10% body weight). Therefore, we performed a micobacterium-PCR on lymph nodes, Intradermal reaction and more serologic investigations looking for an infectious disease. Those investigations showed the presence of atypical mycobacterium DNA in the granuloma. The intradermal reaction was negative. Bartonella Henselae IgG were very high (>4000) but IgM were normal (<1:1000). Given the absence of proved malignancy, the improvement of symptoms and CRP normalisation, we considered, for this patient, owner of two cats, the diagnosis of disseminated Bartonellosis as most probable. The patient was followed after one week with no treatment. The symptoms disappeared and he regained

weight spontaneously. After two weeks, the rectal lesion, all lymphadenopathies and the hepatic abscess disappeared on the pelvic MRI and thoraco-abdominal Ct-scan. One new hepatic lesion appeared in the VI segment. After one month, the patient had no symptoms and one last abdominal CT-scan showed no residual lesion. Discussion: Cat scratch disease (CSD) is an infectious disease caused by Bartonella Henselae, a gram-negative coccobacillus. Though it frequently presents in children, adults can be infected. Clinical manifestations are usually fever and regional lymphadenopathy. Disseminated disease occurs in 5 to10% of cases and is described with abdominal, thoracic, hepatic, splenic, cutaneous and neurologic involvement. No rectal nor mesorectal localisation was ever reported. Conclusion: The atypical and unique presentation in this case of disseminated CSD, mimics a metastatic lower rectal tumour and illustrates that we cannot perform a neoadjuvant treatment for lower rectal cancer without histological proof of malignancy.

- C05 -

NOT SO SWEET. V. Bouillon (1), A. Cremer (1), R. Chapusette (2), T. Gustot (1), D. Franchimont (1) / [1] Hopital Universitaire Erasme, Brussels, Belgium, Gastroenterology, [2] Hopital Universitaire Erasme, Brussels, Belgium, Radiology.

Case Report: A 62-year-old man presented at the emergency department with fever, diarrhea, cutaneous rash and vomiting for 5 days following a trip to Spain. Symptoms appeared after eating fish. Patient is followed at our outpatient clinic for Crohn's disease treated with azathioprine for a few weeks. He is also treated with amlodipine and bisoprolol for high blood pressure. He had neuroendocrine tumor treated by ileocecectomy in the past. The patient is non-smoker and do not consume alcohol. Laboratory test results included the following: C-reactive protein 340 mg/L (<10mg/L), hemoglobin 9.3 g/dl (13-18 g/dl), white blood cells 2.6 x103/mm3 (3.5-11 x103/mm3), platelet count 138 x103/mm3 (>150 x103/mm3), creatinine 2.24 mg/dl (0.6-1.2 mg/dl), GFR 30 mL/min/1.73 m² (> 60 mL/min/1.73 m²), total bilirubin 1.3 mg/dl (<1.2mg/dl), alkaline phosphatase 186 IU/L (53-68IU/L), gamma-glutamyl transferase 153 IU/L (8-61IU/L). After microbiological samples, azathioprine was stopped and empirical antibiotherapy (meropenem and doxycycline) was started due to clinical suspicion of infection such as brucellosis. Clinical deterioration was observed 48 hours after treatment initiation mainly at the respiratory, neurological and cutaneous levels with multiple organ failure (MOF) leading the patient to intensive care unit. A biopsy of one of the papulo-nodular lesions located on the trunk, arms and neck was performed. Thoracic computed tomography scan revealed diffuse septal linear opacities, micronodules and pleural effusions. Autoantibodies, multiple serologies and cultures were negative. After three days of supportive care and without evidence of infection, antibiotherapy was replaced by corticotherapy (1mg/kg). Significant clinical and biological improvement was observed after 24 hours of corticotherapy. Pathology results of skin biopsy revealed neutrophilic proliferation in the superficial dermis and leucocytoclastic vasculitis. We concluded to hypersensitivity syndrome to azathioprine, with sweet syndrome as the main differential diagnosis. Hypersensitivity syndrome to azathioprine leads in rare cases to MOF, and the presence of leucocytoclastic vasculitis has been reported in the litterature in only eight patients to date.

- C06 -

THE GALLBLADDER'S SISYPHEAN TASK RESULTING IN GASTRIC OUTLET OBSTRUCTION. G. Vermeersch (1), N. Cruyt (1), M. Cool (1), G. Deboever (1), J. Geers (2), D. Persyn (1), G. Lambrecht (1) / [1] AZ Damiaan, Oostende, Belgium, Department of Gastroenterology and Digestive Oncology, [2] AZ Damiaan, Oostende, Belgium, Department of General and Abdominal Surgery.

Case Report: At the age of 75 years approximately 35% of women and 20% of men have developed gallstones, roughly 80% of these persons remain asymptomatic. The majority of symptomatic patients present with signs of cholecystitis, cholangitis or pancreatitis [1–3]. Gastro-intestinal obstructions caused by lithiasis, and classically presenting as gallstone ileus, occur in less than 1% of patients with cholecystolithiasis [4]. Gastric outlet obstruction caused by an ectopic gallstone permitted through bilioenteric fistulization, or Bouveret's syndrome, represents only 2-3% of all gallstone related obstructions in the gastrointestinal tract. Only 0.3-5% of gallstones induce bilioenteric fistulas. Predisposing factors are chronic tissue inflammation, increased intravesical pressure and wall ischemia resulting in perforation [1]. Until now only 300 cases have been described in literature [4]. Here we report the case of a 72-year-old male with gastric outlet obstruction caused by a gallstone sized 2.5 cm, which migrated through a cysto-duodenal fistula. The patient presented with complaints of unintentional weight loss over the last 6 months and recurrent vomiting since one week. He was dehydrated and showed signs of malnutrition. Biochemical analysis showed no abnormalities besides an increased level of C-reactive protein (78.7 mg/L; ref. <0.5 mg/L). In the differential diagnosis we included the presence of malignancies (hepatobiliary or upper gastrointestinal tumors). Despite the lower probability, due to normal liver function tests, complicated biliary tract pathology (choledocholithiasis, Mirizzi-syndrome,…) needed to be ruled out as well [5]. Computed tomography (CT) of the abdomen showed signs of cholecystitis and indicated fistulization between duodenum and gall bladder; the gallstone appeared isoattenuated with surrounding tissue. Duodenoscopy revealed the impacted stone. Mechanical lithotripsy with a Soehendra lithotriptor was unsuccessful, therefore the stone was removed by using a stone extraction basket. The patient left our hospital 4 days after admission. A month after discharge C-reactive protein remained elevated, abdominal ultrasound showed persistent signs of calculous cholecystitis. No abnormalities were identified by duodenoscopy. Absence of fistulization was confirmed by Magnetic Resonance Cholangiopancreatography (MRCP). Because of the remaining signs of cholecystitis amoxicillin-clavulanate was initiated, we plan to execute a delayed cholecystectomy. Historically Bouveret's syndrome was associated with mortality risks up to 30%. Improved diagnostic techniques and therapeutic interventions decreased this risk to approximately 12%. Besides significant reported differences in success rate endoscopic intervention (29.0-43%) is generally preferred as first-line therapy above surgery (78.0%). Endoscopic intervention is most successful in stones impacted in the proximal upper gastrointestinal tract (stomach, D1 and D2) (46%) and gallstones ≤4 cm (66%) [6,7]. The most appropriate approach should be considered based on each stone's and patient's individual characteristics. Despite the very low incidence of Bouveret's syndrome, every physician should keep the possibility of gallstone related obstructions in mind when a patient presents with vomiting or unintentional weight loss. Non-specific symptoms and biochemical signs, in combination with possible isoattenuation on radiological images, are significant hazards in the diagnostic process. As the execution of large clinical trials will be almost impossible due to the low incidence of Bouveret's syndrome further sharing of our (un)successful experiences will remain crucial in the future. REFERENCES [1] Haddad FG, Mansour W, Deeb L. Bouveret's Syndrome: Literature Review. Cureus 2018;10. https://doi.org/10.7759/CUREUS.2299. [2] Stinton LM, Myers RP, Shaffer EA. Epidemiology of Gallstones. Gastroenterol Clin NA 2010;39:157–69. https://doi.org/10.1016/j.gtc.2010.02.003. [3] Gurusamy KS, Davidson BR. Gallstones. BMJ 2014;348. https://doi.org/10.1136/BMJ.G2669. [4] Osman K, Maselli D, Kendi AT, Larson M. Bouveret's syndrome and cholecystogastric fistula: a case-report and review of the literature. Clin J Gastroenterol 2020;13:527–31. https://doi.org/10.1007/S12328-020-01114-7. [5] Mees C, de Clerck F. Het syndroom van Mirizzi gecompliceerd door galsteenileus. Tijdschrift voor Geneeskunde 2020; 76:111-116. [6] AL-Habbal Y, Ng M, Bird D, McQuillan T, AL-Khaffaf H. Uncommon presentation of a common disease - Bouveret's syndrome: A case report and systematic literature review. World J Gastrointest Surg 2017;9:25. https://doi.org/10.4240/WJGS.V9.I1.25. [7] Ong J, Swift C, Stokell BG, Ong S, Lucarelli P, Shankar A, et al. Bouveret Syndrome: A Systematic Review of Endoscopic Therapy and a Novel Predictive Tool to Aid in Management. Journal of Clinical Gastroenterology, 54(9), 758-768. https://doi.org/10.1097/MCG.0000000000001221.

- C07 -

THREE CASES OF ACUTE LIVER INJURY AFTER COVID19 VACCINATION. L. HULST (1) / [1] AZ Sint-Maarten, Mechelen, Belgium, gastroenterology.

Case Report: Given the rising need for COVID19 vaccination during the current pandemic, it is important to stay vigilant for any adverse events that may occur. We present 3 cases of acute liver injury seen after a COVID19 vaccination. Other causes were ruled out with imaging (ultrasound/MRI) and extensive biochemical analysis (viral and auto-immune screening). Other drug induced liver injury (DILI) was not suspected. Liver biopsy was not performed in any of the cases. In our 3 patients liver injury seemed to improve or resolve spontaneously with time. The only plausible cause seemed to be a recent COVID19 vaccination. Case 1: a 71-year-old woman of asian origin, with a medical history of breast cancer, presented with flatulence and belging. Standard biochemical blood analysis showed elevated liver enzymes (ALT, AST and GGT; all < 7xULN). Previous liver tests before any COVID19 vaccinations were normal. During follow-up we noticed a further increase of the liver enzymes and highly elevated bilirubin with development of jaundice. Hepatitis screening (viral and auto-immune) and hepatic imaging was negative. There were no recent medication adjustments. Extensive anamnesis learned that the patient had a booster vaccination (Pfizer) 5 days before the rise in liver tests. Looking back at the lab results taken by her general practitioner three months after the second vaccination (Pfizer), we also noticed a mild hepatitis. There was a spontaneous decrease of the liver tests after one week. Case 2: a 59-year-old woman, without relevant medical history, presented with fatigue and pain in the right upper quadrant with an episode of dark urine after recent COVID19 vaccination (first vaccine, AstraZeneca). Biochemical analysis 10 days after vaccination showed elevated liver enzymes, mainly cholestatic (GGT 7xULN, alkaline phosphatase 4xULN), without elevated bilirubin. Viral hepatitis screening was negative. Anti-nuclear antibody was positive, with negative identification. Given a normal IgG, ASM and anti-LKM there were insufficient arguments for an auto-immune hepatitis. An association with the COVID19 vaccination was suspected. There was a spontaneous decrease of the liver tests after one month. Case 3: a 53-year-old woman who had a liver transplantation for porfyria in 2017, presented with elevated liver enzymes (ALT 3xULN, AST < 2xULN, GGT < 2xULN) during follow-up. Immunosupression levels were adequate. Viral screening including CMV PCR was negative. There were no recent medication adjustments. The patient had her second COVID19 vaccine (AstraZeneca) 13 days before the first elevated ALT value. A spontaneous decrease of the liver function tests was seen. Additional imaging with MRI is still planned given a stenosis of the biliary anastomosis in the past. Tabel 1: maximum values liver tests AST (U/L) ALT (U/L) GGT (U/L) Alk phosphatase (U/L) Total bili (mg/dL) Direct bili (mg/dL) Case1 750 1009 1298 467 15.4 11.4 Case2 51 99 268 429 0.57 0.29 Case 3 54 115 43 88 0.31 <0.10 Further research is necessary to verify a causal relationship between COVID19 vaccination and acute liver injury. With the need for (multiple) booster vaccinations in mind, it is important to be aware of this possible adverse event.

SHIGELLOSIS: A NOT-TO-BE-OVERLOOKED STD IN MSM. M. Van Herck (1), F. Gillis (1), F. Couturier (1), S. Nullens (1), P. Steger (1) / [1] GZA Sint-Vincentius ziekenhuis, Antwerpen, Belgium, Gastroenterology.

Case Report: Case 1: A 33-year-old man with a history of syphilis and sporadic use of antiretroviral pre-exposure prophylaxis before high-risk sexual encounters presented with a two-day history of bloody diarrhea, abdominal cramps and fever. On further questioning the patient reported unprotected anal intercourse with multiple men two days before the onset of his symptoms. Lab results showed no leukocytosis (6.100/µL) and a high CRP (182mg/L). He was hospitalized for treatment of severe dysentery and empirical antibiotic treatment was started with intravenous amoxicillin/clavulanic acid 1000/200mg q.i.d. Rectosigmoidoscopy showed an ulcerative rectosigmoiditis with purulent discharge and vesicular lesions in the colon. Pathology showed signs of acute colitis with cryptitis without signs of dysplasia or CMV infection. Fecal cultures were positive for Shigella flexneri and antibiotic susceptibility testing showed resistance to amoxicillin acid and susceptibility to levofloxacin, cefotaxime, and cotrimoxazole. Blood cultures remained negative. Serology for HIV, hepatitis B and C were negative. Additional rectal swab was positive for Neisseria gonorrhea. The treatment with amoxicillin/clavulanic acid was substituted for a one-time dose of ceftriaxone 1gr via intramuscular injection and 1gr of oral azithromycin, followed by oral azithromycin 500mg once daily for the two following days, thus treating both S. flexneri and N. gonorrhea. Under this treatment a rapid clinical and biochemical evolution was observed and the patient was discharged two days after admission. Case 2: A 32-year-old man with a history of an anal Neisseria gonorrhea infection and sporadic use of antiretroviral pre-exposure prophylaxis before high-risk sexual encounters, presented with a four-day history of fever, watery diarrhea, and vomiting. The patient mentioned previous sexual contact with men but denied recent sexual encounters. Lab results showed leukocytosis (22.300/µL), a high CRP (352mg/L) and elevated transaminases (AST 127U/L, ALT 114U/L). He was hospitalized for severe dysentery and empirical antibiotic treatment was started with intravenous amoxicillin/clavulanic acid 1000/200mg q.i.d. Rectosigmoidoscopy showed no abnormalities. Pathology showed moderate inflammation without disruption of crypt architecture, signs of dysplasia or CMV infection. Ultrasound and MRCP at admission showed an acalculous cholecystitis accompanied by ascites. Fecal cultures were positive for Shigella sonnei and antibiotic susceptibility testing showed multi-drug resistance to amoxicillin, levofloxacin, cefotaxime, erythromycin, and cotrimoxazole, and susceptibility to meropenem. Blood cultures remained negative. Serology for HIV, syphilis, hepatitis B and C were negative. Amoxicillin/clavulanic acid was substituted for intravenous meropenem 1gr t.i.d., which was continued for seven days. A favorable clinical and biochemical evolution was observed and no signs of cholecystitis were present on an ultrasound at discharge. These two cases illustrate different ways of presentation of a Shigella infection in men who have sex with men (MSM) and present several learning points. Shigella are Gram-negative pathogenic enterobacteria that are transmitted through contaminated food or water, as well as via sexual oral–anal contact, especially in MSM. S. sonnei is the most common pathogen causing shigellosis in Belgium, accounting for 75% of the documented infections. However, the 2020 annual report from the Belgian National Reference Centre for Shigella describes a remarkable decrease in documented S. sonnei cases in favor of S. flexneri, making S. flexneri the dominant subgroup accounting for 51% of cases. Importantly, recent studies have shown that the more pathogenic S. flexneri is becoming the dominant subgroup in MSM in Canada and England and case 1 raises the question whether a shift from S. sonnei to S. flexneri in the Belgian MSM subpopulation is ongoing. Moreover, both cases highlight the increasing prevalence of multi-drug-resistant S. sonnei in Belgian MSM, with resistance to one first-line agent (i.e., azithromycin, ciprofloxacin, and ceftriaxone) in 33% and to two first-line agents in 25% of cases, as described by a recent study by Fischer et. al. Another important aspect is the co-occurrence of other sexually and orofecally transmitted diseases. Accordingly, active screening and treatment for Chlamydia trachomatis, Neisseria gonorrhea, HIV, syphilis, hepatitis A-B-C, Entamoeba spp., and Giardia lamblia should be performed. Lastly, case 2 demonstrates an important Shigella-associated acalculous cholecystitis, which resolved completely with antibiotic therapy, without the need for surgical intervention.

STAUFFER SYNDROME: SOMETHING TO KEEP IN MIND. J. Vandewinckele (1), L. Harlet (2) / [1] Ghent University, Ghent, Belgium, Gastroenterology, [2] AZ Delta, Roeselare, Belgium, Gastroenterology.

Case Report: Paraneoplastic hepatopathy was first described in 1961. It is also known as Stauffer's syndrome and it's predominantly associated with renal cell carcinoma (RCC). Over time, it has been reported in cases of prostatic carcinoma, bronchogenic tumor and lymphoproliferative diseases. It is characterized by an elevated alkaline phosphatase, aminotransferases and prolonged prothrombin time. Mainly, it presents without jaundice, but a rare variant of Stauffer's syndrome manifested by jaundice has been reported. Therapy is based on disease control and depends on the underlying malignancy. Stauffer's syndrome is yet to be fully understood. This syndrome should be considered in patients with unexplained hepatic cholestasis in the absence of hepatobiliary disease. Here we present a case of a 76-year-old patient with a rare variant of Stauffer's syndrome owing to renal cell carcinoma, which was diagnosed during an evaluation for enigmatic hepatic cholestasis. In this case, cholestasis was the first systemic clinical manifestation of paraneoplastic disease.

CROHN DISEASE ONSET IN A PATIENT TREATED WITH IL-17 INHIBITOR FOR REFRACTORY PSORIASIS. M. Abdessalami (1), M. Zeriouh (1), A. Cremer (1), C. Liefferinckx (1) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology.

Case Report: A 33-year-old Maghrebian patient presented to our outpatient clinic with epigastric abdominal pain, bloating, diarrhea, and anorexia for 3 months with a weight loss of 18kg. He has a significant smoking addiction with a consumption of about 20 cigarettes per day. His past medical history is marked by a latent tuberculosis treated in 2013 with isoniazid and rifampicin. Since 2016, the patient suffers from a severe psoriasis refractory to multiple treatments (methotrexate, ciclosporin, ustekinumab and guselkumab) for which a treatment with brodalumab (IL-17 Inhibitor) was started 5 months ago. It should be noted that his mother is affected by Crohn's disease. The blood panel demonstrated iron deficiency anemia (hemoglobin :12.6 g/dL) and an inflammatory syndrome with a C-reactive protein of 25 mg/L and neutrophilic leukocytosis (15,000/mm³). Stool cultures with bacteriological and parasitic research were negative. An abdominal computed tomography scan showed extended terminal ileitis (+/- 40 cm) and, to a lesser extent, colitis of the ascending colon. Gastroscopy revealed a hiatus hernia and helicobacter pylori positive atrophic gastritis, while ileocolonoscopy showed deep serpiginous non-hemorrhagic ulcerations in the terminal ileum. Biopsies confirmed the presence of inflammatory lesions of the ileal mucosa compatible with the diagnosis of Crohn's disease which was retained and classified A2 B1 L3 according to Montreal classification. Considering symptoms onset of Crohn's disease two months after the initiation of treatment with Brodalumab, it was stopped and corticotherapy was initiated. After multidisciplinary consultation meeting with the dermatology department, infliximab was started in combination with azathioprine with rapid clinical and biological improvement. Efficacy and safety of IL-17 inhibitors have been demonstrated in the treatment of psoriasis in numerous clinical trials. However, in recent years, many cases of exacerbation or induction of IBD have been reported in the literature. When prescribing these treatments, the risk/benefit balance should be discussed with the patient, especially if there are associated risk factors for developing Crohn's disease such as family history or smoking status. In such patients, physicians have to keep in mind the digestive side effects of anti-IL-17 and should carefully and quickly assess any new digestive symptoms with faecal calprotectin or even by gastroscopy and colonoscopy. References: 1) Paradoxical gastrointestinal effects of interleukin-17 blockers. Ann Rheum Dis. 2020 Sep;79(9):1132-1138. doi: 10.1136/annrheumdis-2020-217927. 2) A Randomized, Double-Blind, Placebo-Controlled Phase 2 Study of Brodalumab in Patients With Moderate-toSevere Crohn's Disease. Am J Gastroenterol. 2016 Nov;111(11):1599-1607. doi: 10.1038/ajg.2016.298.

- G01 -

USING THE ESGE QUALITY CHECK APP IN A NON-ACADEMIC ENDOSCOPY UNIT: HOW MUCH DOES IT COST AND WHAT ARE THE BARRIERS? S. Bourseau (1), B. Bastens (1), R. Bisschops (2), P. Leclercq (1) / [1] Clinique Mont Legia - CHC Groupe Santé, Liège, Belgium, Gastroenterology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology.

Introduction: The European Society of Gastrointestinal Endoscopy (ESGE) has developed performance measures (PM) for upper gastrointestinal (UGI) endoscopy and established a framework for quality assessment in Europe. Implementation of PMs may face several barriers in daily routine endoscopy, including lack of motivation and/or resources. Furthermore, human resources required for this task are unknown. ESGE QIC developed recently an online tool, the ESGE QIC Quality Check App (QIC app) to assist endoscopy units to measure quality PMs.
Aim: The aim of this survey was to assess the human resource as an allocated time analysis and potential barriers for disseminating and implementing performance measures in UGI endoscopy in a non-academic endoscopy unit, using the QIC app.
Methods: In one non-academic endoscopy unit (12 endoscopists; mean age: 44y, 31-59), PM from 300 successive UGI endoscopy reports were first entered into the QIC app to calculate the pre-training performance of the unit. In parallel, we adapted the existing semi-structured electronic reporting system, integrating ESGE PM and landmarks image capturing. During a training meeting, we presented to the endoscopists the results of the pre-training audit, the detailed concept of PM for UGI endoscopy and the adapted electronic reporting system. After a 2-weeks test phase, PM implementation started. After a 3-month implementation phase, we re-assessed PM of 300 successive UGI endoscopy reports from the same operators (post-training test). Barriers for implementation were assessed by a questionnaire to the endoscopists after post-training audit. We calculated human resources (time-allocation) needed for implementation of the quality project.
Results: The evolution of PM pre- and post-training is: Fasting instructions prior to UGI endoscopy (KPM1) increased from 0 to 100% (target: 95%). Documentation of procedure duration (KPM2) increased from 0 to 84% (target: 90%). Accurate photodocumentation of anatomical landmarks and abnormal findings (KPM3) increased from 0 to 82% (target: 90%). Accurate application of standardized disease-related terminology (KPM4) increased from 93 to 98% (target: 95%). Application of Seattle protocol in Barrett's surveillance (KPM5) increased from 20 to 75% (target: 90%). Accurate registration of complications after therapeutic UGI endoscopy (KPM6) increased from 0 to 39% (target: 95%). Minimum 7-minute procedure time for first diagnostic UGI endoscopy and follow-up of gastric intestinal metaplasia (mPM1) increased from 0 to 67% (target: 90%) Minimum 1-minute inspection time per cm circumferential Barrett's epithelium (mPM2) increased from 0 to 37.5% (target: 90%). Use of Lugol chromoendoscopy in patients with a curatively treated ENT or lung cancer to exclude a second primary esophageal cancer (mPM3) could not be calculated because absence of such indication in the post-training sample (target: 90%). Application of a validated biopsy protocol to detect gastric intestinal metaplasia (MAPS guidelines) (mPM4) increased from 82 to 97% (target: 90%). Prospective registration of Barrett's patients (mPM5) increased from 0 to 100% (target: 85%). Although both KPM and mPM improved after 3 months, only 2 KPM (1&4) and 2 mPM (4&5) reached the minimum target. IT resources time-cost was 26 hours, electronic reporting system adaptation time-cost was 14 hours, team training time-cost was 13 hours and data encoding time-cost (pre- and post-training audit on QIC App) was 38 hours (i.e. 91 hours in total). In the post-training questionnaire, most frequently reported barriers for implementing PM in digital reports were not user-friendly of electronic endoscopy reporting software for integrating PM (8/12), lack of time during reporting process (8/12), resistance to change (3/12), lack of binding regulation (1/12).
Conclusions: Our analysis showed a reasonable time allocation for implementation of UGI PMs using the ESGE QIC app. In particular, after training and minimal adaptation of the IT system, a service audit with a sample of 300 UGI can be performed in less than 3 working days. Since this is required only once a year, this seems a reasonable price in human resources. Proper electronic reporting system integrating user-friendly PM reporting and automated PM extraction are the cornerstone for facilitating implementation of PM in endoscopy.

- G02 -

LOCAL INJECTION OF TRIAMCINOLONE ACETONIDE WITH SELECTED ADD-ON ORAL STEROIDS THERAPY AFTER EXTENSIVE ESOPHAGEAL ENDOSCOPIC SUBMUCOSAL DISSECTION TO PREVENT POST-ESD STRICTURE: FIRST REPORT OF A PROSPECTIVE VALIDATION PROTOCOL IN WESTERN COUNTRIES. D. Carpentier (1), G. Englebert (1), A. Bucalau (1), L. Verset (2), P. Demetter (2), P. Eisendrath (1), J. Deviere (1), A. Lemmers (1) / [1] CUB Hôpital Erasme, Belgium, Gastroenterology, Hepatopancreatology and Digestive Oncology, [2] Institut Jules Bordet, Brussels, Belgium, Pathology.

Introduction: Endoscopic submucosal dissection (ESD) has spread worldwide for treatment of superficial esophageal lesions. However, without preventive measures, this technique is associated with 70-100% post-endoscopic esophageal stricture, especially after more than 75% circumference resection. Single local injection of triamcinolone acetonide (TA) at the end of procedure has been demonstrated to prevent post-ESD esophageal stricture for resections of less than 90% of circumference in Japan. Oral corticosteroids are used in addition to TA injection for resections reaching up 90-100% of circumference. In Western countries, the most used treatment consists of oral steroids with tapering doses for 7-8 weeks with risks of systemic steroids complications. To our knowledge, there is no Western data on the use of triamcinolone injection for esophageal stenosis prevention.
Aim: Assess efficacy of a systematic preventive stricture protocol for esophageal ESD.
Methods: We prospectively collected data from patients who underwent esophageal ESD in Erasme Hospital (Brussels, tertiary center) from January 2016 to October 2021. Degree of mucosal defect was evaluated at the end of the resection and specimen size measured after being pinned on cork. Local injection of 50 milligrams of TA was systematically done for mucosal defect superior to 50% circumference. Moreover, patients with at least 90% circumference resection received local injection of TA followed by oral corticosteroids treatment (during 7 weeks with tapering dose). Primary outcome was the evaluation of stenosis after 28 days. Secondary outcomes included the mean number of balloon dilation sessions and the rate of refractory stenosis. Adverse events after local injection of triamcinolone were noted. Stricture rate was evaluated before eventual further radiofrequency ablation (RFA) of Barrett. Post-RFA strictures were not taken into account.
Results: A total of 92 consecutive patients underwent 105 esophageal ESD procedures. The median age was 69 years [36-98] and 66% were male. Indications comprised 40% squamous cell carcinoma, 55% Barrett or adenocarcinoma lesions and 5% others. The median resection specimen size was 40 mm [10-130 mm] with an "en-bloc" resection rate of 99% and a complete endoscopic resection rate of 98%. Histopathological analyses showed a R0 rate of 80%. The median percentage of mucosal defect circumference was 50% [20-100%]. Degree of mucosal defect was classified in 3 categories: resection of less than 50% (50 ESDs), 50 to 90% (48 ESDs) and more than 90% (7 ESDs). 49 patients received TA local injection alone and 9 patients received both local and oral corticosteroids. No adverse events were observed after local injection of triamcinolone. Among all ESD procedures, one patient benefited from an early esophagectomy (20 days after ESD procedure) and was then ruled out of esophageal stenosis assessment. Follow-up was available in 91 patients after a median of 599 days [29-1912 days]. In total, we observed post-ESD esophageal strictures in 9 patients (global rate of 8.6 %) : 5/48 (10%) strictures for the 50-90% of mucosal defect circumference group and 4/7 (57%) for more than 90% group. Altogether, stricture rate for more than 50% circumference resection was 16% (9/55) and 20% (5/25) for more than 75% circumference resection. Symptomatic esophageal strictures were treated by endoscopic balloon dilation. The median time before first dilation session was 42 days [27-82 days]. The mean number of balloon dilation sessions was 6 [2-17] with a mean dilation caliber of 16.5 mm. Two patients needed 3 or more dilation sessions with an 18 mm diameter balloon and were considered as refractory stenosis managed by esophageal stent placement.
Conclusions: ESD allows "en-bloc" resection of superficial esophageal lesions with clear margins with no technical limit in terms of size lesion. However, clinical limits are oncologic indication and risk of secondary stricture. Local TA injection for all patients that underwent an ESD with a mucosal defect of more than 50% of the circumference, with added oral corticosteroids for those with more than 90%, led to a very low stricture rate in our prospective cohort. As a single session treatment without long-term potential systemic side effects, it appears beneficial to use this strategy for our patients in Western countries.

- G03 -

FEASIBILITY OF IMPLEMENTING THE USE OF REGULAR ARRANGEMENT OF COLLECTING VENULES IN DAILY ENDOSCOPY PRACTICE WITHOUT PREVIOUS TRAINING: EARLY RESULTS FROM A PROSPECTIVE OBSERVATIONAL STUDY. G. Rasschaert (1), L. Vandermeulen (1), M. Schils (1) / [1] Universitair Ziekenhuis Brussel, Brussels, Belgium, Gastroenterology and Hepatology department.

Introduction: Identification of regular arrangement of collecting venules (RAC) has been proposed as an accurate tool for detection of Helicobacter pylori (Hp) negative patients. So far its use is not recommended in international guidelines. And it is not yet implemented widespread in daily endoscopy practice. Although suggested by experts to be easy to, one of the potential barriers is the supposed necessity of training for this type of optical diagnosis.
Aim: Our aim was to review the reliability of implementing RAC in daily endoscopy practice only by conceptual knowledge of its existence, without dedicated previous training. The presence of star-like venules in the lesser gastric curvature is considered RAC+. Its absence or irregularity is determined RAC-.
Methods: Data from all esophagogastroduodenoscopies with biopsies for Hp screening were collected prospectively for six months. Our institution mainly serves patients from the metropolitan area of a midsize Western European capital with an ethnically diverse population. High-definition endoscopes without magnification, applying white light, were used. Exclusion criteria were a history of (distal) gastrectomy, gastric bypass and active upper gastrointestinal bleeding. Three operators with different level of overall endoscopy experience (two, three and ten years) participated. Hp status was confirmed by gastric biopsy (2x antrum, 2x corpus). Pathologists were blinded to the RAC status.
Results: One hundred and thirty-two patients were included from May 2021 through October 2021. 61 (46.2%) were determined RAC+, while 71 (53.8%) were nominated RAC-. The prevalence of Hp infection was 37.1% (49 patients).

The absence of RAC was associated with Hp infection in 46 out of 71 patients, with PPV of 64.8% for the diagnosis of Hp infection. In contrast, 58 out of 61 RAC+ patients were free of Hp infection, with NPV of 95.1% for the exclusion of Hp infection. Of all 49 Hp positive patients, 46 displayed a negative RAC pattern, correlating with a high sensitivity of 93.9%. These results correspond to suggested values stated in literature. There was variation between operators, without significant outliers.
Conclusions: The presence of RAC+ in the lesser curvature can accurately identify patients without Hp infection. Our preliminary data suggests that thorough training in RAC might be redundant. Rapid implementation by untrained operators seems feasible as the global performance in our study matched data in previous literature. The main limitation of this study is the reduced sample size. Our findings are hypothesis generating and need to be confirmed in a larger group of operators.

- G04 -

BALLOON-ASSISTED ENTEROSCOPY AND MOTORIZED SPIRAL ENTEROSCOPY: COMPETITIVE OR COMPLEMENTARY TECHNIQUES? T. Moreels (1), L. Monino (1), P. Deprez (1), H. Piessevaux (1) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Hépato-Gastroentérologie.

Introduction: The motorized spiral enteroscope (MSE) is a newly designed enteroscope with a motorized spiral overtube allowing deep and even complete enteroscopy in patients with normal anatomy. Balloon-assisted enteroscopy was developed 20 years ago, first the double-balloon enteroscope, followed by the single-balloon enteroscope (SBE). These enteroscopes can be used to perform antegrade and retrograde enteroscopy, to complete colonoscopy when conventional colonoscopy fails and to perform ERCP in patients with surgically altered anatomy. There are no studies comparing the efficacy of MSE and SBE.
Aim: To compare technical efficacy of MSE and SBE consecutively performed in the same patient.
Methods: All patients who underwent enteroscopy using both SBE and MSE were retrospectively analysed for technical success. In case of a failed procedure, defined as not able to obtain the clinical objective of the procedure, enteroscopes were switched during the same procedure. In case of a repeat procedure, defined as a second enteroscopy performed at a later date as indicated on clinical grounds, the type of enteroscope used was retrieved from the patient's medical file. The most efficient enteroscopy technique was identified based on the insertion depth, as mentioned in the endoscopy report. All enteroscopies were performed under fluoroscopic control, allowing visual comparison of insertion depth. MSE was performed with the PSF-1 enteroscope, SBE was performed with the SIF-Q180 or the XSIF-180JY enteroscope.
Results: In 2 years time, a total of 28 patients underwent enteroscopy using both SBE and MSE. The male/female ratio was 11/17 with a mean age of 61±3 years (range 18-89). SBE and MSE were both used as starting enteroscope in 14 patients each. Antegrade enteroscopy was the most frequently performed procedure (67%), followed by retrograde enteroscopy in 11%, endoscopy of the excluded stomach after Roux-en-Y gastric bypass in 11% and ERCP after Roux-en-Y liver transplantation in 11%. Based on the enteroscope insertion depth, MSE was considered the best technique in 12/28 patients (43%), SBE in 32% and in 7 patients (25%) both enteroscopy techniques were considered equally effective (p=0.35, Chi-square). In the current analysis, the enteroscopy route and the type of surgical reconstruction were not correlated with the technical success of either of the enteroscopy systems. However, MSE tended to fail in patients with sharply angulated small bowel limbs, irrespective of previous abdominal surgery.
Conclusions: This head-to-head comparison of insertion depth of motorized spiral enteroscopy to single-balloon enteroscopy revealed that MSE is superior to SBE in 43%, equal to SBE in 25% and inferior to SBE in 32% of the patients in this relatively small group of patients who underwent repeat enteroscopy using both techniques. MSE allows deeper and even complete enteroscopy, also in patients with surgically altered anatomy, but fails mainly in case of sharply angulated small bowel limbs. A possible explanation may lie in the different endoscope design: MSE has the same diameter as a colonoscope and the tip behaves like a colonoscope, whereas SBE has the same diameter as a gastroscope with similar angulation properties of the tip. These results illustrate that MSE and SBE are complementary rather than competitive enteroscopy techniques.

- G05 –

THE ACCURACY OF HUMAN DETECTION OF SUBMUCOSAL INVASIVE CANCER – ANALYSIS OF 739 INDIVIDUAL ASSESSMENTS OF LARGE NON-PEDUNCULATED COLORECTAL POLYPS (LNPCPS) USING A NOVEL CLINICAL DECISION SUPPORT TOOL. L. Debels (1), C. Schoonjans (1), A. Hoorens (2), L. Desomer (3), J. Anderson (4), R. Valori (5), D. Tate (1) / [1] Universitair ziekenhuis Gent, Belgium, Gastroenterology, [2] Universitair ziekenhuis Gent, Belgium, Pathology, [3] AZ Delta, Roeselare, Belgium, Gastroenterology, [4] Cheltenham General Hospital, United Kingdom, Gastroenterology, [5] Gloucestershire Royal Hospital, United Kingdom, Gastroenterology.

Introduction: Correct management of large non-pedunculated colorectal polyps ≥ 20mm (LNPCPs) is guided by the accurate discrimination of whether they harbour submucosal invasive cancer (SMI). Current tools to achieve this goal are complex and often poorly understood. This leads to incorrect decision making (e.g. piecemeal resection of SMI necessitating surgery or surgery for benign disease) and the associated negative outcomes for patients.
Aim: We developed a simple online clinical decision support tool via expert consensus, based on the demarcated area principle – where a regular pit/vascular pattern becomes disordered - to search for OVERT (visible on the surface) SMI and 4 characteristics of LNPCPs (Paris classification, size, colonic location, and granularity) to quantify the risk for COVERT (hidden) SMI.
Methods: An online survey was sent to gastroenterologists and trainees consisting of a 10-minute educational video with 20 subsequent randomly presented standardized videos of LNPCPs. Participants' first impression (Blink impression) was requested prior to viewing the tool on the presence of SMI within the shown polyp. Participants were then asked to use the clinical decision tool to classify polyps as low, high (COVERT risk), or very high risk (OVERT risk) of SMI. Participant responses were compared to expert responses and histopathologic data. Clinical relevance of participant scoring was based upon the determination of using piecemeal endoscopic mucosal resection versus en-bloc endoscopic resection or surgery.
Results: 739 individual responses were analysed amongst 37 participants. Blink impression predicted absence of SMI with high negative predictive value (NPV) - 97.5% (95% confidence interval (95% CI): 95.0 – 99.0%) and good accuracy 72.3% (95% CI: 68.9 – 75.6%). Participants ruled out the presence of an expert-determined demarcated area (OVERT SMI) with a high NPV - 97.6% (95% CI: 96.0 – 99.0%). Lower accuracy [78.6% (95% CI: 76.5 - 81.5%)] resulted from overcalling of a demarcated area by participants (38.6% vs 20%). The accuracy of participant determination of (COVERT characteristics) size, Paris classification, granularity, and location (given in the survey) were 66.3% (95% CI: 61.8 - 70.5%), 66.3% (95% CI:61.8 - 70.5%), 64.8% (95% CI: 60.3 - 69.1%) and 94.8% (95% CI: 92.4 - 96.6%) respectively. The overall accuracy of the resultant participant score (compared to expert) was 66.2% (95% CI: 62.6 - 69.6%). When considering the clinical relevance of decisions that would result from the scores given by participants, correct treatment would result in 71.3%, undertreatment in 13.1% and overtreatment in 15.6% (table 1). Overtreatment was in expert assigned low risk polyps where participants designated them high (1.1%) or very high risk (24.8%). Undertreatment was in expert assigned high risk polyps where participants designated them low risk (59.2%) and very high risk (25.2%). Qualitative data suggested that the tool was easy to use.
Conclusions: Endoscopists of varying experience can reliably exclude SMI within LNPCPs from a standardized video using an online clinical decision support tool after a short training intervention. Further validation and application of this tool in clinical practice may prevent the negative patient consequences of missing SMI or over-detection of SMI during real-time assessment of LNPCPs.

- G06 -

LOW RISK OF LOCAL RECURRENCE AFTER A SUCCESSFUL EN BLOC ENDOSCOPIC SUBMUCOSAL DISSECTION FOR COLORECTAL LESIONS WITH POSITIVE HORIZONTAL RESECTION MARGINS (R-ESD STUDY). M. Figueiredo Ferreira (1), K. Haasnoot (2), F. Baldaque-Silva (3), A. Koch (4), J. Santos-Antunes (5), E. Dias (5), M. Omae (3), L. Van Tilburg (4), H. Dang (6), J. Boonstra (6), L. Moons (2), A. Lemmers (1) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology, Hepatopancreatology and Digestive Oncology, [2] University Medical Center Utrech, The Netherlands, Gastroenterology and Hepatology, [3] Karolinska Institutet, Karolinska University Hospital, Sweden, Endoscopy, Department of Upper Gastrointestinal Diseases, [4] Erasmus MC, University Medical Center Rotterdam, The Netherlands, Gastroenterology and Hepatology, [5] University Hospital São João , Porto, Portugal, Gastroenterology, [6] Leiden University Medical Center (LUMC), Leiden, The Netherlands, Gastroenterology and Hepatology.

Introduction: A positive or indeterminate horizontal resection margin (HM1) after polypectomy of colorectal polyps warrants intensive endoscopic follow-up as it is associated with an increased risk of local recurrence. In comparison to polypectomy, colorectal endoscopic submucosal dissection (ESD) has the advantage of continuous optical control during the mucosal cut. Furthermore, an HM1 after ESD may be caused by cauterization, suboptimal embedding technique, or tangential cutting at the pathology department. This makes it unclear whether an HM1 imposes a risk of local recurrence after ESD in cases of en bloc resection. The European Society of Gastrointestinal Endoscopy (ESGE) guideline for ESD advises colonoscopy at 3-6 months after HM1, but also states that this recommendation is based on low-quality evidence. We hypothesized that the recurrence rate after a complete ESD for colorectal lesions with positive horizontal resection margins (HM1) is not increased compared to free resection margins (HM0) resections.
Aim: We aim to test whether a positive horizontal resection margin after a complete en bloc ESD is predictive for local recurrence.
Methods: This study was a multicenter, multinational observational prospective cohort study. Patients were identified from the individual prospective ESD databases of multiple referral centers for endoscopic resection of large colorectal neoplasia, including the Karolinska Institute Stockholm (Stockholm, Sweden), Erasme Hospital (Brussels, Belgium), São João University Hospital Center (Porto, Portugal), and three centers from the Netherlands: Erasmus MC (Rotterdam), Leiden University Medical Center (Leiden), and University Medical Center Utrecht (Utrecht). The inclusion criteria were a complete ESD for a colorectal lesion (en bloc and macroscopic radical resection as judged by the endoscopist),

with patients having had at least one follow-up endoscopy. Patients with positive vertical resection margin, non-adenoma origin, or additional surgical resection were excluded. Lesions with submucosal invasion (T1) without high-risk features were included if margins were free of carcinoma. Consecutive patients meeting the inclusion criteria were selected from the prospective databases from 2011 to 2020. Cases and controls were defined by a horizontal resection margin positive or indeterminate for dysplasia (HM1) or a free resection margin (HM0), respectively. The main outcome was local recurrence, with a minimum follow-up length of 6 months for all patients.
Results: From 928 consecutive ESDs (2011-2020), 354 patients (40% female, mean age 67 years) were included concerning 308 non-invasive lesions (HM0 n=212, HM1 n=96) and 46 T1 lesions (HM0 n=38, HM1 n=8). Median follow-up time was 15.5 months (IQR 6.7-32.0) and was equal for HM0 and HM1 (15.5 vs. 15.5 months; p=0.907). An HM1 resection was significantly associated with longer duration, larger size (both endoscopic and pathologic report), ≥ 50% circumferential involvement, and difficult access to the polyp. Recurrence rate for non-invasive lesions was 1/212 (0.5%; 95%CI 0.08-2.6%) for HM0 vs. 1/96 (1.0%; 95%CI 0.02-5.7%) for HM1 during a median follow up of 16.4 months. Recurrence rate for T1 lesions was 0/38 (0.0%; 95%CI 0.0-9.1%) for HM0 vs. 2/8 (25%; 95%CI 7.2-59%) for HM1 during a median follow-up of 11.9 months. Both recurrences were located in the rectum and classified as T3 with lymph node metastasis within 9 months of initial resection.
Conclusions: In this multicenter European cohort study including the largest number of complete colorectal ESD cases with a positive horizontal resection margin published so far, we found that, for non-invasive lesions, the risk of recurrence within 12 months after a complete ESD with positive horizontal resection margins is very low and equal to an ESD with clear horizontal margins. Postponing the first follow-up endoscopy to 12 months after initial resection might be justified in this context. The same could not be confirmed for low-risk T1 colorectal cancer with positive horizontal resection margins.

- G07 -

PAIRED WORKING COMBINED WITH ON-DEMAND DIRECT EXPERT SUPERVISION ALLOWS A SAFE AND EFFECTIVE IMPLEMENTATION OF RECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION IN A NON-ACADEMIC REFERRAL HOSPITAL. G. Bastens (1), O. Plomteux (1), N. Blétard (2), P. Demaret (3), R. Bisschops (4), V. Lepilliez (5), P. Leclercq (1) / [1] Clinique Mont Legia - CHC Groupe Santé, Liège, Belgium, Gastroenterology, [2] Clinique Mont Legia - CHC Groupe Santé, Liège, Belgium, Pathology, [3] Clinique Mont Legia - CHC Groupe Santé, Liège, Belgium, Intensive Care Unit, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [5] Hôpital Privé Jean Mermoz - Lyon, Lyon, France, Gastroenterology.

Introduction: Endoscopic submucosal dissection (ESD) achieves en-bloc resection of superficial digestive neoplasms without any size limit, reducing the risk of local recurrence. ESD is a demanding technique with a long learning curve, long procedure time and increased risk of complications. These limitations first slowed the widespread of ESD in the West, where rectal lesions are usually first approached in the learning curve. ESD training and implementation have been addressed by European Society of Gastrointestinal Endoscopy (ESGE). Once ESD proficiency achieved, ESGE recommends a minimum case load of 25 ESD procedures per year. Working in an alternating operators' pairs has never been evaluated. This strategy could be an alternative way to reach minimal case load.
Aim: We evaluated the efficacy and the safety of rectal ESD implementation in a non-academic referral hospital performed in operator pairs associated with on-demand direct expert supervision.
Methods: This is a retrospective analysis of the 90 first consecutive rectal ESDs performed between 2013 and 2021 in one non-academic referral hospital performed by two operators working in pairs (OP, PL), trained similarly to the current ESGE ESD curriculum (animal model training followed by referral center observation fellowship and ten first human ESD procedures done under expert supervision). After this training period, operators started rectal ESD as a duo, switching every 30' during the same procedure. On-demand direct expert supervision (VL) was requested when procedure was anticipated to be more complex. The first half (P1) was compared to the second half of the series (P2). "Supervised" were compared to "unsupervised" procedures. Endpoints included: rates of en-bloc/R0/curative resection, complications, ESD speed, 3- and 12-months recurrence rate.
Results: 90 patients (mean age: 68 years) underwent rectal ESD (mean ESD specimen surface: 1581 mm2). Final histology was: LGD (44), HGD (19), Adenocarcinoma (pTis: 13, sm1: 4, sm2: 7, T2: 1), NET: 2. En-bloc/R0/curative resection was respectively achieved in 96.7/84.4/80% of overall. En-bloc/R0/curative resection was achieved respectively in 97.6/81/78.6% of "supervised" subgroup (P1+P2) and 95.8/87.5/83.3% of "unsupervised" subgroup (P1+P2). Post-ESD bleeding rate was 3.3% (three cases in P1-supervised group), perforation rate was 2.2% (one in P1-unsupervised, one in P2-supervised) and one stenosis (in P2-supervised). All complications were managed conservatively with no need for surgery. There is no significant difference (p>0.05) in en-bloc/R0/curative resection rates between P1 and P2 or "supervised" and "unsupervised" subgroups. ESD speed slightly increased over time in the "unsupervised" group reaching > 9cm2/h (8.5cm2/h for P1 vs 9.2 cm2/h for P2, p>0.05) without increase in complication rate. en-bloc/R0/curative resection rates was 93.3/80/80% in P1 unsupervised group, reaching 97/90.9/84.8% in P2 unsupervised group. P1 compared to P2 showed lower need of expert supervision with a gradual inversion of supervised/unsupervised ratio over time (66.7% vs 26.7%, p<0.05). There was no recurrence at 3- and 12-months follow-up when data available (72/90 at 3-mo; 44/90 at 12-mo).
Conclusions: Working in pairs combined with on-demand direct expert supervision allows effective implementation of rectal ESD in a non-academic referral center with safe gradual transition to autonomy.

- G08 -

EUS-GUIDED GASTROENTEROSTOMY VERSUS DUODENAL STENTING FOR MALIGNANT GASTRIC OUTLET OBSTRUCTION: AN INTERNATIONAL, MULTICENTER, PROPENSITY SCORE-MATCHED COMPARISON. M. Bronswijk (1), R. Van Wanrooij (2), G. Vanella (3), P. De Gooyer (2), W. Laleman (1), H. Van Malenstein (1), F. Mandarino (3), G. Dell'anna (3), P. Fockens (2), P. Arcidiacono (3), S. Van Der Merwe (1), R. Voermans (2) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] Amsterdam UMC, Amsterdam, The Netherlands, Department of Gastroenterology and Hepatology, [3] Vita Salute San Raffaele University, Milan, Italy, Pancreatobiliary Endoscopy and Endosonography Division.

Introduction: Endoscopic duodenal stenting (ES) is the current standard treatment for malignant gastric outlet obstruction (GOO) in patients with limited life expectancy. ES is however prone to stent dysfunction. EUS-guided gastroenterostomy (EUS-GE) has emerged as a novel technique with potentially improved efficacy, although comparisons with ES have remained scarce.
Aim: Our aim was to compare efficacy, safety and dysfunction rates of EUS-GE and ES in patients with malignant GOO using propensity-score matching.
Methods: We conducted an international multicenter retrospective analysis of consecutive patients undergoing either EUS-GE or ES for GOO between 2015 and 2021 in 3 European centers. Primary outcomes were clinical success (GOO scoring system (GOOSS) ≥2) and stent dysfunction (GOOSS≤1 after initial clinical success). A propensity score-matched (1:1) analysis was performed using age, sex, underlying disease, disease stage, ascites and peritoneal carcinomatosis as variables, with a maximum propensity score difference of 0.05.
Results: A total of 214 patients were identified, who underwent either EUS-GE (107) or ES (107). After propensity-score matching, 176 patients (88 in each group) were matched and compared. Technical success rates for EUS-GE and ES were 94.3% vs. 97.7%, respectively (p=0.44). Clinical success rates were 90.9% vs. 75.0% (OR=3.33 [95%CI=1.39-8.00], p=0.008). After a median follow-up of 85 days (IQR 43-157) in the EUS-GE group and 57 days (IQR 18.5-130.5) in the ES group, recurrent GOO occurred in 1/80 (1.3%) EUS-GE patient due to stent migration, and was observed in 17/66 ES patients (25.8%) (OR=0.04; 95% CI=0.01-0.28 p<0.001). Median time to stent dysfunction was 243 days after EUS-GE and 57 days (IQR 27-169.5) after ES (p=0.222). Kaplan-Meier analysis showed higher probability of dysfunction free survival for EUS-GE (HR=27.4. [95%CI 4.2-28.2], p<0.001) with a 6-months' probability of remaining recurrence-free of 100% versus 65.0% in ES. Adverse events occurred in 9/88 (10.2%) patients after EUS-GE and in 18/88 (20.5%) patients after ES (OR=0.44; 95%CI=0.19-1.05 p=0.093). The adverse events in EUS-GE existed of infectious complications (aspiration pneumonia (n=1; 1.1%) or cholangitis (n=3; 3.4%)), bleeding (n=1; 1.1%), post-procedural pain (n=1;1.1%), and in three cases (3.4%) intraperitoneal LAMS maldeployment resulted in emergency salvage surgery. Adverse events after ES comprised of infectious complications including aspiration pneumonia (n=4; 4.5%), cholangitis (n=4; 4.5%), post-procedural pain (n=4; 4.5%), bleeding (n=3; 3.4%), atrial fibrillation (n=1; 1.1%) and stent migration (n=1; 1.1%). Median survival after EUS-GE was 85 days (43-157) vs. 57 days (18.5-130.5) after ES (p=0.080).
Conclusions: When compared to enteral stenting, EUS-GE resulted in higher clinical success and lower stent dysfunction rates with similar safety. These data suggest that EUS-GE may be preferred over ES in patients with malignant GOO.

- G09 -

SAFETY AND EFFICACY OF DOUBLE EUS-BYPASS VERSUS SURGICAL HEPATICOJEJUNOSTOMY AND GASTROJEJUNOSTOMY. M. Bronswijk (1), J. Lauwereys (1), H. Van Malenstein (1), W. Laleman (1), J. Jaekers (2), H. Topal (2), B. Topal (2), R. Kunda (3), S. Van Der Merwe (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Visceral Surgery, University Hospitals Gasthuisberg, KU Leuven, Belgium, [3] University Hospital Brussels, Vrije Universiteit Brussel, Belgium, Department of Surgery, Department of Gastroenterology and Hepatology, Department of Advanced Interventional Endoscopy.

Introduction: Both gastric outlet obstruction (GOO) and biliary obstruction may occur simultaneously in patients with gastrointestinal malignancies. Small series have suggested that same-session double EUS-bypass is feasible. However, in this specific context, no comparisons with surgery have been published to date.
Aim: Our aim was to analyze our experience using same-procedure double EUS-bypass and compare outcomes with open surgical hepaticojejunostomy and gastrojejunostomy (SHG).
Methods: A tertiary single-center retrospective analysis was performed of all consecutive double EUS-procedures performed for GOO and biliary obstruction from 2018 to March 2021 (local study identifier: S65484). Consecutive historical surgical controls were extracted from the institutional database. All EUS procedures were performed under

general anesthesia, using an electrocautery-enhanced lumen apposing metal stent and the WEST technique, whereas for biliary obstruction EUS-guided hepaticogastrostomy (HG), rendez-vous (RV), choledocho-duodenostomy (CDS) or antegrade stenting (AS) were allowed.
Results: In total, 42 patients were identified (female 57.5%, mean age 63±10.3 years, pancreatic cancer 62.5%), of which 12 patients (28.6%) were treated with double EUS-bypass and 30 patients with SHG (71.4%). Considering EUS-biliary drainage, 3 HG and 2 CDS were performed, as well as 6 AS and 1 RV. At baseline, the EUS group exhibited a higher median Charlson Comorbidity Index (9.0 [IQR 7.0-10] vs. 6.5 [IQR 5.0-8.0], p=0.011) and showed a trend towards higher expected anesthesiology risk (ASA IV: 16.7% vs. 0.0%, p=0.077). Technical success was achieved in 11 out of 12 EUS-treated patients (91.7%) vs. 100% in the SHG group (p=1.000). Per protocol clinical success, defined as a GOOS score >2 and serum bilirubin decrease >50%, was achieved in 81.8% and 80.0% respectively (p=1.000). In the EUS group, median procedure time (81 [IQR 63.5-85.8] vs. 95min [IQR 90.0-122.5], p=0.019) and median time to oral intake (1.0 [IQR 1.0-1.8] vs. 6.0 day(s) [IQR 5.3-9.8], p<0.001) were significantly shorter compared to patients undergoing surgery. Using the ASGE lexicon for adverse events (AE), the total number of AE was similar in both groups (5 [41.7%] vs. 15 [46.7%] events, p=1.000), with an even distribution in severe (1 [8.3%] vs. 7 [23.3%] events, p=0.402), moderate (2 [16.7%] vs. 5 [16.7%] events, p=1.000) and mild AE (2 [16.7%] vs. 1 [3.3%] event(s), p=0.192). One fatal AE occurred in the surgical group. Although safety and efficacy seemed similar, median hospital stay was significantly shorter in the EUS group (11.0 [IQR 8.3-12.8] vs 23.0 [IQR 13.0-35.5] days, p=0.001), while dysfunction rates (10% vs. 13%, P=1.000) and median overall survival were comparable (83 [IQR 39-306] vs. 303 [IQR 98-511] days, p=0.095).
Conclusions: Despite being used in a patient population with more comorbid conditions and more advanced disease stage, double EUS bypass achieved similar efficacy and safety, as well as shorter hospital stay and time to oral intake, when compared to surgery. The challenges of achieving complete biliary drainage in patients with advanced disease using EUS only, may have played a role in the current safety outcomes. Although future efforts should be directed towards further optimizing outcomes of double EUS-bypass procedures, the current results underline the usefulness of EUS in this specific context.

- G10 -

EUS GUIDED GASTROENTEROSTOMY: EVOLUTION OF THE TECHNIQUE TO IMPROVE TECHNICAL SUCCESS (WITH VIDEO). L. Monino (1), T. Moreels (1), J. Gonzalez (2), H. Piessevaux (1), M. Barthet (2), P. Deprez (1) / [1] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, Gastroenterology, [2] Assistance Publique des hôpitaux de Marseille, Hôpital Nord, Marseille, France, Gastroenterology.

Introduction: The creation of a functional anastomosis between the stomach and the jejunum has long time been an exclusively surgical intervention. Recently, endoscopic ultrasound guided gastroenterostomy (EUS-GE) is possible using a lumen apposing metal stent (LAMS). Initially, the EUS-GE was proposed for indications of malignant gastric outlet obstruction (GOO). The improvement or modification of some steps of this procedure has improved the technical success and reduced the complication rate. As improvements have been made, the indications for EUS-GE have expanded to include benign pathologies.
Aim: To compare feasibility and safety of different techniques to perform EUS-GE.
Methods: Data of all EUS-GE performed in two centers (UCLouvain and AP-HM Marseille) during 2014-2021 were collected and analyzed: age, sex, procedure time, technique used for identification of target limb, technique used for creation of EUS-GE, technical success, procedural adverse events, post-procedural adverse events. All procedures were performed using CO2 insufflation under general anesthesia and with fluoroscopic control. Technical success of EUS-GE with LAMS was defined as the creation of gastroenterostomy using only the LAMS (without salvage therapy).
Results: 42 patients (mean age 63 years; male: 20) underwent 44 EUS-GE procedures. The rate of GOOs for benign pathologies was 31% (13/42). Regardless of the technique used, the rate of creation of the EUS-GE with LAMS was 80% (32/44). Procedural adverse events rate was 27,3% (12/44). In case of misdeployment of the LAMS (11), salvage therapy of the anastomosis was achieved in 54.5% of the cases (6/11). The most commonly used techniques in this cohort were enteroclysis/needle puncture with guide wire (33) and orointestinal drain/direct puncture with electrocautery LAMS (11). The technical success rate of the EUS-GE with LAMS was 66.7% (22/33) for the enteroclysis/needle puncture with guide wire versus 91% (10/11) for the orointestinal drain/direct puncture with electrocautery LAMS. The technical success of EUS-GE after salvage therapy increased to 81.8% and 100% respectively. Clinical success, whatever the technique, was 100% (38/38) at one week and one month. Post procedural adverse events rate was 10.5 % (one peritonitis, one delayed bleeding, one stent overgrowth and one infection). There was no mortality related to EUS-GE.
Conclusions: The orointestinal drain/direct puncture with electrocautery LAMS technique for performing a EUS-GE seems to be the most reliable, fastest and simplest method. In addition, there are fewer adverse events using this technique compared to the needle guidwire technique. Prospective studies are needed to confirm these encouraging results.

- G11 -

EUS-GUIDED TRANSRECTAL DRAINAGE OF PELVIC ABSCESSES: A RETROSPECTIVE ANALYSIS OF 16 PATIENTS. H. Peeters (1), M. Simoens (2), J. Lenz (2) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, gastroenterology, [2] ZNA Jan Palfijn, Merksem, Belgium, gastroenterology.

Introduction: Pelvic abscess is a common complication of abdominal surgery or intestinal or gynecological diseases. Over the last decades, endoscopic ultrasound (EUS)-guided drainage has emerged as a minimally invasive alternative to percutaneous or surgical treatment of pelvic abscesses.
Aim: To evaluate safety and efficacy of EUS-guided transrectal pelvic abscess drainage in a single center.
Methods: From February 2017 to October 2021, all data on patients who were treated for pelvic abscesses by EUS-guided drainage in a single center, were retrospectively analyzed.
Results: A total of 16 patients were treated for pelvic abscesses by EUS-guided drainage. The procedure was technically successful and uneventful in all 16 patients (100%). Etiology of the abscess was postsurgical (n=4, 24%), secondary to medical illness (n=10, 63%) or gastrointestinal perforation (n=2, 13%). The abscess was multilocular in 5 patients (31%), the mean largest diameter was 79 mm (range 47-146 mm). Drainage was performed using 2 double pigtail stents, and in 1 patient an additional 10 Fr drainage catheter was deployed. Two patients (13%) required a second endoscopic intervention. Treatment success, defined by complete abscess resolution on follow-up CT scan along with symptom relief, was 100%. There was no need for surgical intervention. The median post-procedural hospital stay was 5 days. No recurrence was reported within a median time of follow-up of 26 months.
Conclusions: EUS-guided transrectal drainage of pelvic abscesses using double pigtail stents is safe and highly effective. This case series contributes to the cumulative evidence that, in expert hands, EUS-guided drainage should be considered as first-line approach for treatment of pelvic abscesses.

- G12 -

PERFORMANCE AND APPLICABILITY OF A FIRST GENERATION SINGLE-USE DUODENOSCOPE: A SINGLE-CENTER COHORT STUDY. H. Van Malenstein (1), D. Persyn (2), A. Schuermans (3), M. Dreesen (4), W. Meert (4), K. Buysschaert (1), S. Van Der Merwe (1), W. Laleman (5) / [1] University Hospitals Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] AZ Damiaan, Oostende, Belgium, Department of Gastroenterology and Hepatology, [3] University Hospitals Leuven, Belgium, Department of Infection Control and Epidemiology, [4] University Hospitals Leuven, Belgium, Department of Pharmaceutical and Pharmacological Sciences, [5] Univeristy Hospitals Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Multidrug resistant organisms (MDRO) represent an emerging global public health threat. In the context of endoscopy, duodenoscopes used for endoscopic retrograde cholangiopancreatography (ERCP) are most prevalent and notorious for scope contamination and thus for exogenous patient-to-patient duodenoscope-related infections (DRIs). Despite standardization and optimization of disinfection protocols, DRIs remain an emerging threat for patients undergoing ERCP. Single-use duodenoscopes could represent a potential alternative avenue to circumvent the problem of reprocessing and thus risk of exogenous patient-to-patient transmission.
Aim: In this study we tested the feasibility and technical success rate of a recently made available single-use duodenoscope.
Methods: The usability, performance and safety of a recently developed single-use duodenoscope was evaluated in a cohort of patients scheduled for ERCP. In this single center study clinical data were collected (e.g. indications for ERCP, ERCP specific maneuvers, ASGE grade of complexity etc) and a standardized evaluation of scope performance was executed. Subjective performance rating scores were given to ERCP maneuvers (options include not preferred/neutral/preferred relative to the reusable duodenoscope). In addition, device performance characteristics were scored ranging from a Likert scale of 1 [not preferred] to 5 [comparable to prior historical experience with reusable duodenoscope]) and median overall satisfaction. Outcomes included performance ratings of the single-use duodenoscopes, adverse events (assessed at 3 days and 1 week), and crossover rate to reusable duodenoscopes.
Results: Performance of single-use duodenoscopes was evaluated in 52 consecutive patients. The ERCP completion rate with a single-use duodenoscope was 90,4%, after cross-over to reusable duodenoscope 94,2%. The mean ASGE grade was 2,7 with 27 procedures (51,9%) considered as advanced level complexity (ASGE grade 3 & 4). Performance rating showed that 94% of the therapeutic treatments were assessed comparable to when using a traditional reusable duodenoscope. We scored 14 specific options of ERCP maneuvers. Most of the ratings were neutral (141/148, 95,3%) when comparing the single-use duodenoscope with the reusable duodenoscope. Only 7 (4,7%) maneuvers were labeled as not preferred. We also documented performance characteristics for 23 ERCP maneuvers. 17 maneuvers (73,9%) had a median score of 5 (comparable to prior historical experience with reusable duodenoscope). Navigation/pushability/torquability of the scope, range of motion, selective cannulation and tip deflection were appreciated slightly less than with a reusable duodenoscope. Overall satisfaction amounted to 80%. No major adverse events were experienced related to the use of the single-use endoscope.

Conclusions: Single-use duodenoscopes can provide an alternative to avoid the intensive and often inconsistent results of cleaning and disinfection procedures. We confirm feasibility, adequate performance characteristics and safety over a broad range of ERCP procedures, both in terms of indication and complexity, of a recently developed first-generation single-use duodenoscope.

- G13 -

DYE ANOTHER DAY: DYE-BASED CHROMOENDOSCOPY VERSUS I-SCAN VIRTUAL CHROMOENDOSCOPY IN LONG-STANDING UC: A MULTICENTER PROSPECTIVE RANDOMIZED CONTROLLED TRIAL. A. Jans (1), P. Sinonquel (2), M. Pierik (3), T. Seerden (4), S. Sloth (5), J. Karstensen (6), G. De Hertogh (7), I. Demedts (2), H. Willekens (8), S. Vermeire (2), R. Bisschops (2) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Internal Medicine, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [3] Maastricht University Medical Centre, Maastricht, The Netherlands, Gastroenterology, [4] Amphia Hospital Breda, Breda, The Netherlands, Gastroenterology, [5] Copenhagen University Hospital – Herlev and Gentofte, Hellerup, Denmark, Gastrounit, [6] Copenhagen University Hospital - Amager and Hvidovre, København, Denmark, Gastrounit, [7] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Pathology, [8] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Endoscopy.

Introduction: Long-standing ulcerative colitis (UC) has an increased risk for developing colorectal dysplasia and neoplasia. Dye-based chromoendoscopy (DCE) and virtual chromoendoscopy (VCE) increase detection of neoplastic lesions. However, limited data are available on the impact of i-scan VCE for UC neoplasia detection.
Aim: We undertook a prospective randomized controlled trial to compare the neoplasia detection between DCE and i-scan in patients with long-standing UC.
Methods: In 4 European hospitals, 136 patients with long-standing UC (mean disease duration 19.88 (DCE) vs 18.49 years (i-scan)) were randomized (1:1) to either DCE with methylene blue 0.1% (n=71) or i-scan (n=65). Biopsies were taken from visible lesions and surrounding mucosa. Neoplastic lesions were defined as any type of dysplasia, adenoma, sessile serrated polyp or carcinoma. Statistical analysis was performed using t-test for continuous data and Fishers' exact for comparison of proportions.
Results: The neoplasia detection rate was not significantly different between the DCE (18.3%) vs VCE (26.2%) group, respectively (OR 0.63, 95%CI 0.27 – 1.37, p=0.305). However, the per lesion neoplasia detection was significantly better with i-scan than with DCE (14.5% vs 33.9%, p=0.033). The mean number of neoplastic lesions per colonoscopy was 0.24 for DCE and 0.32 for i-scan (p=0.432). Both withdrawal and total procedural time were on average 10.1 and 9.8 minutes shorter in the i-scan group (p<0.001).
Conclusions: This multicenter prospective randomized trial showed that in long-standing UC patients, no significant difference in neoplasia detection was found between DCE and i-scan. However, i-scan had a lower false positive rate and a significant shorter procedure time. I-scan could therefore be a valid replacement for DCE.

- G14 -

PREDICTION OF RESIDUAL NEOPLASIA AFTER A NON-CURATIVE COLORECTAL ESD: A MULTICENTRIC AND MULTINATIONAL STUDY. M. Figueiredo Ferreira (1), M. Pioche (2), F. Ramos-Zabala (3), P. Cecinato (4), F. Gallego (5), P. Barreiro (6), C. Félix (6), S. Sferrazza (7), F. Berr (8), A. Wagner (8), E. Albéniz (9), H. Uchima (10), R. Küttner-Magalhães (11), C. Fernandes (12), R. Morais (13), S. Gupta (14), M. Marques (13), M. Bourke (14), G. Macedo (13), A. Lemmers (15), J. Santos-Antunes (13) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology and Digestive Oncology, [2] Edouard Herriot Hospital, Lyon, France, Hepatology and Gastroenterology, [3] University Hospital HM Montepríncipe, Madrid, Spain, Gastroenterology, [4] Azienda USL - IRCCS di Reggio Emilia, Reggio Emilia, Italy, Gastroenterology and Digestive Endoscopy Unit, [5] Hospital de Poniente, Almería, Spain, Gastroenterology and Digestive Endoscopy Unit, [6] Centro Hospitalar Lisboa Ocidental, Lisbon, Portugal, Gastroenterology, [7] Santa Chiara Hospital, Trento, Italy, Gastroenterology and Digestive Endoscopy Unit, [8] University Clinics Salzburg - Paracelsus Medical University, Salzburg, Austria, Internal Medicine I, [9] Complejo Hospitalario de Navarra, Navarrabiomed Research Institute, Public University of Navarra, Pamplona, Spain, Gastroenterology, [10] Hospital Universitario Germans Trias i Pujol, Barcelona, Spain, Gastroenterology, [11] Centro Hospitalar do Porto, Porto, Portugal, Gastroenterology, [12] Centro Hospitalar Vila Nova de Gaia/Espinho, VN de Gaia, Portugal, Gastroenterology, [13] University Hospital São João , Porto, Portugal, Gastroenterology, [14] Westmead Hospital, Sidney, Australia, Hepatology and Gastroenterology, [15] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology, Hepatopancreatology and Digestive Oncology

Introduction: Endoscopic Submucosal Dissection (ESD) in the colorectum allows an en-bloc resection irrespective of the size and morphology of the lesion allowing precise pathological evaluation and lower recurrence rate compared to piecemeal EMR. Nevertheless, a significant number of ESDs do not complete all the predefined requisites for being considered curative. The best management strategy following colorectal non-curative ESDs (NC-ESDs) is still under debate, since those different requisites may not carry the same independent risk for lymph node metastasis (LNM) or residual lesion.
Aim: Our goal was to evaluate all the consecutive colorectal NC-ESDs performed in several western centers, assessing the rate of residual lesion in the surgical specimen or during the endoscopic follow-up, as well as the rate of LNM in patients submitted to surgery, in order to establish new predictive scores for these outcomes.
Methods: We performed an international multicentric analysis of prospectively collected data concerning all consecutive cases of colorectal ESD performed in 14 centers from Europe (Portugal, Spain, France, Belgium, Italy and Austria) and Australia, between November 2009 and December 2020. All patients with NC-ESDs (with positive or undetermined resection margins, deep submucosal invasion (>SM1), lymphovascular invasion or tumour budding) that were submitted to complementary surgery or had at least one follow-up endoscopy were included. ESD failure was an exclusion criterion.
Results: From 2214 colorectal ESDs, 340 were included in the study. These comprised 133 (39%) T1 cancers, 34 (10%) Tis lesions and 91 (27%) HGD lesions, 74 (21%) LGD, 6 (2%) serrated and, finally, 2 (1%) rectal squamous cell cancer lesions (which were excluded). Residual lesion was observed in 40 (12%) patients overall. Surgery was performed in 99 patients, and 76 (77%) had neither residual lesion nor LNM in surgical specimen. From the patients not submitted to surgery (n=241), only 17 (7%) presented residual lesion, during a mean endoscopic follow-up time of 25 months. Regarding only the malignant invasive lesions (n=133), 24 (18%) showed a residual lesion (20 in the surgical specimen and 4 during endoscopic follow-up). Among those that were submitted to surgery (n=95), the rate of LNM or residual lesion in the wall for SM1 cancers was 0%. For colorectal cancer with deeper submucosal invasion, there was a 20% rate of residual lesion; however, in those lesions without any other risk factors the risk of LNM or residual lesion in the wall was also 0%. Independent risk factors for LNM were poor differentiation (p=0.002) and lymphatic permeation (p<0.001). The independent risk factors for the presence of residual lesion in the wall were colonic location (vs rectum, p=0.047) and positive vertical margin (p=0.042). After a ponderation of each factor's impact, the NC-Lymph score and NC-Wall score were created to help better predict the risk of LNM and residual lesion, respectively. Among patients with malignant lesions that did not undergo surgery (n=38), 4 (11%) showed residual, benign lesions in the scar (treated by endoscopic resection techniques) and 9 received additional treatment (chemotherapy and/or radiotherapy). Regarding benign lesions, KAR/ hybrid technique was associated with residual lesion (p=0.041). None of the other risk factors, including piecemeal resection (p=0.189) or HM+/HMx (p=1.000) were related with the presence of residual lesion during follow-up. Piecemeal resection as a risk factor was only significant in HGD/Tis lesions (p=0.003), not in LGD.
Conclusions: In this large, multicenter western study, none of the patients with a NC-ESD of a SM1 T1 colorectal cancer had residual lesion in the wall or in the lymph nodes, even with the presence of other high-risk criteria. Similarly, >SM1 T1 cancers without any other risk factors did not present residual lesion in the follow-up. Among >SM1 T1 cancer patients, lymphatic permeation or poor differentiation in the ESD specimen were the only independent factors for LNM, and its presence should warrant surgery. Lesions situated in the colon and without free vertical margin have the highest risk of residual lesion in the wall. The developed scores can be a useful tool in clinical practice and in further clinical trials.

- G15 -

DEVELOPMENT AND VALIDATION OF THE GLOBAL POLYPECTOMY ASSESSMENT TOOL (GPAT) - A NOVEL ONLINE ASSESSMENT TOOL FOR ANY COLORECTAL POLYPECTOMY. A. De Crem (1), D. Tate (2), L. Desomer (2) / [1] Ghent University, Ghent, Belgium, Medicine, [2] University Hospital Ghent (UZ Gent), Gent, Belgium, Maag-, darm- en leverziekten.

Introduction: Colorectal polypectomy is commonly incompletely performed with high variability between endoscopists resulting in interval cancer or repeated procedures. Existing scores to assess polypectomy technique are cumbersome and difficult to use. We developed an online assessment tool for any colorectal polypectomy: the Global Polypectomy Assessment Tool (GPAT).
Aim: We aimed to validate this tool with endoscopists of varied experience through demonstrating the inter-rater agreement.
Methods: GPAT was developed using statements derived from a Delphi-consensus between 11 internationally recognized polypectomy-experts. The score has 20 items and calculates an overall quality score and a complexity score. Evidence-based statements and explanatory videos enhance the reliability of the score. We included nine endoscopic-view videos of polypectomies and recruited twelve international assessors (4 gastro-enterologists, 2 surgeons, 3 trainees and 3 medical students) via email. The videos were assessed in random order after watching a 2 minute 37 second explanatory video of GPAT. The assessors scored the SMSA-score and GPAT-criteria for each video. The inter-rater agreement was calculated with the Fleiss Kappa-value (κ)).
Results: We analyzed 108 GPAT-assessments of 12 assessors. Moderate agreement was demonstrated for the target population (gastroenterologists κ: 0.413 95%CI [0.348-0.478] and trainee gastroenterologists κ: 0.460 95%CI [0.360-0.560]). The surgeons and medical students demonstrated fair agreement (respectively κ: 0.381 95%CI [0.226-0.537] and κ: 0.248 95%CI [0.134-0.362]). Moderate agreement was found when analyzing the SMSA-scores separately for the gastroenterologists (κ: 0.415 95%CI [0.095-0.735] and trainee-gastroenterologists (κ: 0.518 95%CI [0.043-0.993]). Positive feedback was received regarding content and ease of use.

Conclusions: This validation demonstrates standardized scoring of colorectal polypectomy quality and difficulty with moderate inter-observer agreement amongst a varied panel of gastroenterologists and trainee-gastroenterologists with similar agreement found for the broadly used SMSA-score. With further study, GPAT may allow standardized assessment of trainees' polypectomy competency with feedback on performance, demonstration of improvement over time and a method to accredit endoscopists in different levels of polypectomy.

- G16 -

A ONE-DAY VIRTUAL-LIVE HYBRID TRAINING COURSE IS FEASIBLE AND HAS A POSITIVE IMPACT ON COLONOSCOPY KEY PERFORMANCE INDICATORS (KPI) AMONGST EXPERIENCED ENDOSCOPIC TRAINEES. L. Krott (1), L. Debels (1), C. Schoonjans (1), R. Valori (2), J. Anderson (3), L. Desomer (4), D. Tate (1) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology, [2] Gloucestershire Hospitals NHS Foundation Trust, United Kingdom, Gastroenterology, [3] Cheltenham General Hospital, United Kingdom, Gastroenterology, [4] AZ Delta, Roeselare, Belgium, Gastroenterology.

Introduction: Colonoscopy is a complex practical skill, which is highly operator dependent. The consistent attainment of key performance indicators (KPIs) by a colonoscopist depends primarily upon training. Local factors, outside of a trainee's control, may mean their training is unstructured and contingent upon the observed practice of a small number of trainers. This is particularly true given current travel restrictions imposed by the worldwide COVID-19 pandemic.
Aim: We sought to demonstrate the feasibility and impact of a one-day virtual-live colonoscopy-training course with remote, experienced trainers.
Methods: 6 endoscopy trainees [Belgium] underwent a one-day (8-hour) course (the intervention) involving training by consciously competent colonoscopists who were physically remote [United Kingdom]. The intervention comprised 5 interactive sessions on colonoscopy theory combined with 6 live sessions, where trainees performed colonoscopy in their local endoscopy unit, receiving real-time instruction and performance enhancing feedback via a tele-conference monitor situated next to the endoscopic image. Trainers and the five trainees not doing the colonoscopy could follow the procedure in real-time including room view, view of the magnetic colonoscope imager and the endoscopic image. Colonoscopy KPIs were assessed on trainee-performed colonoscopies [unsedated or midazolam/fentanyl sedation] for 3 weeks prior and 4 weeks after the training. Qualitative trainee and trainer feedback regarding the course was obtained.
Results: 6 experienced colonoscopy trainees (median 26 months prior-training) underwent the intervention. Trainees performed 60 colonoscopies, (33 pre-, and 27 post-training). Favorable trends in cecal intubation rate (CIR) and adenoma detection rate (ADR) were observed, (91% vs 96% (P=0.386), and 39% vs 63% (P=0.069) respectively). A trend to improved endoscopist-reported comfort scores ([Gloucester Comfort Score (GCS)>3] 18% vs 11% (P=0.375)) and nurse-reported comfort scores (GCS>3 22% vs 8% (P=0.189)) was observed (Table 1). Course participants and trainers alike reported globally favourable qualitative experiences with the expert trainers finding the format feasible and specifically mentioning they could focus on the training without distraction due to reduced cognitive load.
Conclusions: Standardization of colonoscopy training is critical to the consistent attainment of KPIs by practicing colonoscopists and improving patient experience. This is the first demonstration of delivering live colonoscopy training remotely: an approach acceptable to trainees and trainers that has a positive impact on KPIs. Pending larger studies focused on efficacy, this approach has the potential to create a standardized curriculum for colonoscopy training, removing the barriers of travel, and allowing expanded exposure to consciously-competent expert trainers.

- G17 -

DEVELOPMENT AND VALIDATION OF A NOVEL SCORE FOR THE COMPLETENESS OF CAECAL INTUBATION SCORE – THE CCIS (COMPLETENESS OF CAECAL INTUBATION SCORE). L. Crapé (1), L. Debels (2), C. Schoonjans (3), L. Desomer (4), J. Anderson (5), R. Valori (5), D. Tate (1) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Department of Gastroenterology and Hepatology, [2] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology and Hepatology, [3] AZ St. Jan Brugge AV, Brugge, Belgium, Department of Gastroenterology and Hepatology, [4] AZ Delta, Roeselare, Belgium, Department of Gastroenterology and Hepatology, [5] Cheltenham General Hospital, United Kingdom, Department of Gastroenterology and Hepatology.

Introduction: Colonoscopic screening leads to a reduction in colorectal cancer incidence through the detection and removal of the precursors of colorectal cancer (CRC). However, 5- 10% of CRCs are post-colonoscopy CRC (PCCRC), defined as CRC within 3-36 months of a previously normal colonoscopy. As reported before by Stoffel et al, post-colonoscopy cancers are more likely to be located in the proximal colon [OR: 1.92 (95% CI 1.36, 2.72)]. A potential explanation could be because of failed caecal intubation or incomplete caecal visualisation. Key performance indicators (KPIs) in colonoscopy have been implemented to improve this. Photo-documentation of caecal landmarks has been suggested as a colonoscopy KPI but no validated score exists to define its completeness.
Aim: To create and validate the Completeness of Caecal intubation Score (CCIS) as a potential new colonoscopy key performance indicator.
Methods: To create the CCIS, the caecum was divided into eight parts; appendiceal orifice (AO), tri-radiate fold part 1 (TF-1), 2 (TF-2), 3 (TF-3) and four outer quadrants (OQ 1-4). The ileo-cacecal valve (ICV) is a reference point but is not part of the score. OQ1 is adjacent to the valve, the three other quadrants are labelled clockwise from this quadrant. For every component of the CCIS present on the image, one point is gained with a maximum possible CCIS of 8. Endoscopists of varying backgrounds and education were contacted using a survey to assess anonymous the same 20 image-sets of caecal intubation (presented in a random order) after having watched an instructional video. They were asked their subjective first impression (yes/no) regarding completeness of caecal intubation and a subjective percentage they believed was assessed. They were then asked to fill the score defining which of the eight components of CCIS were seen using an online tool. Responses were compared between raters (using the two-way mixed effects model of ICC) and to the opinion of the authors derived at a consensus meeting.
Results: Of 1217 contacted, 115 endoscopists responded and 79 of them completed the survey. Most (69,6%) were trained endoscopists, 20,3% were trainees. 8,9% were surgeons or trainee surgeons. CCIS was significantly higher in the images that were classified as completely visualised during first-impression evaluation and had a strongly positive correlation with the subjective stated percentage of the caecum visualised (Pearson correlation 0,83); p<0,001). The overall accuracy of the participant determination of CCIS as compared to author-consensus was 82,3% , 95% confidence interval (CI) 81,7% to 83,0%. The overall inter-rater agreement (ICC) for CCIS was moderate (0,53 [95% CI 0,39-0,71]). For comparison the Boston Bowel Preparation Score (BBPS) interobserver agreement was similarly moderate (0,56 [95% CI 0,42 -0,73]). When looking at the different areas of the caecum, accuracy was overall 69,1% (95% CI 68,3-70,0%). The overall inter-rater agreement ICC for the different areas was 0,35 (95% 0,29-0,42). Agreement on CCIS was higher in the visualisation of AO/TF1,2,3 (ICC=0,34; 95% CI 0,26-0,45) then for the four outer quadrants (ICC=0,26; 95% CI 0,20-0,36). Accuracy of AO/TF1,2,3 was 71,5% (95% CI 70,3-72,6%), compared to the accuracy of the four OQ (66,8% [95% CI 65,6-68,0%]). In particular OQ1 was determined with an higher accuracy of 72,3% (95% CI 70,0-74,5%) as compared to the other three quadrants (accuracy 65,0% [95% CI 63,6-66,4%]). When taking number of images per set into account, inter-rater agreement for multiple images per caecum intubation was higher (ICC=0,40 [95% CI 0,32-0,50]) compared to the ones with only one image (ICC=0,29 [95% CI 0,22-0,39]) per intubation.
Conclusions: Endoscopists of varying experience accurately determined the expert-agreed completeness of cecum intubation score and it was moderately stable amongst raters. This score has the potential to be used as a retrospective KPI and driver of best practice in colonoscopy.

- G18 -

EXPLORATION OF THE EXCLUDED STOMACH IN A PATIENT WITH ROUX-EN-Y GASTRIC BYPASS: HOW TO USE THE MOTORIZED SPIRAL ENTEROSCOPE. T. Moreels (1), L. Monino (1) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Hépato-Gastroentérologie.

Case Report: We present a didactic case video of the endoscopic treatment of a 64-years old male patient with recurrent episodes of melena and need for blood transfusion. He underwent Roux-en-Y gastric bypass 5 years before. Initial work-up with upper and lower gastrointestinal endoscopy was negative, as was the wireless videocapsule examination of the small bowel. He was referred for enteroscopy to examine the excluded small bowel biliopancreatic limb and the excluded stomach as a potential bleeding source. An antegrade motorized spiral enteroscopy was performed and the biliopancreatic limb and the excluded stomach were easily reached. An anastomotic ulcer with stigmata of recent bleeding was identified at the Roux-en-Y anastomosis. It was successfully treated with hemostatic clips. The didactic video demonstrates the preparation, introduction and retraction of the motorized spiral enteroscope in a patient with surgically altered anatomy. It also shows the usefulness of the additional water jet channel while placing hemostatic clips.

- G19 -

ENDOSCOPIC SUBMUCOSAL DISSECTION OF A SOLITARY GASTRIC PLASMOCYTOMA: 'THIRD SPACE ODDITY'. G. Rasschaert (1), P. Gkolfakis (2), P. Eisendrath (3), L. Verset (4), J. Devière (2), A. Lemmers (2) / [1] CUB Institut Jules Bordet, Brussels, Belgium, Gastroenterology and Digestive Oncology department, [2] CUB Hôpital Erasme, Belgium, Gastroenterology, Hepatopancreatology and Digestive Oncology department, [3] CHU Saint-Pierre, Brussels, Belgium, Gastroenterology and Hepatology department, [4] CUB Institut Jules Bordet, Brussels, Belgium, Pathology department.

Case Report: Although well established in classic indications, the use of endoscopic submucosal dissection (ESD) can help to solve some rare clinical situations. A 35-year-old woman without medical history underwent an esophagogastroduodenoscopy for progressive, non-PPI-responding epigastralgia since twelve months. A 10 mm submucosal lesion in the antrum was reported. Biopsies revealed an extramedular plasmocytoma, independently confirmed by expert pathology. Apart from weight loss, attributed to epigastralgia, no other B symptoms were present. Diagnostic work up disclosed a unique gastric hypermetabolic focus on PET-CT. There were no biological anomalies.

Bone marrow biopsy was normal. Endoscopic evaluation, one month after radiotherapy administered with curative intent (40Gy), suggested a non-responding lesion. Endoscopic ultrasound evaluation observed a homogenous, hypoechoic mass (12.0 x 5.7 mm) limited to the submucosa. ESD was proposed as treatment option in a multidisciplinary team. Lesion delineation was obtained using NBI and TXI. ESD was performed by expert hands with a GIF-HQ-190 gastroscope, using a Dual Knife (Olympus®) and Glycerol solution, by conventional technique taking 1cm lateral margins and dissecting alongside the proper gastric muscular layer under near focus and TXI enhancement. “En bloc” resection of a 60 x 40 mm specimen was obtained in 150 minutes. No post-radiotherapy fibrosis was noted. Pathology confirmed the presence of a 21 mm submucosal lambda monoclonal plasmocytoma infiltrating up to 1071 micrometers. Lateral and vertical margins were free, even if free deep submucosa was only 50 micrometers on the specimen. Endoscopic evaluation at six months showed post ESD scarring without signs of relapse, while the patient reported minor residual epigastralgia but regained normal weight. Albeit reassuring, close endoscopic and imaging follow up is proposed. Although rare, ESD (alone or complementary to other treatment modalities) can serve as an adequate treatment option for digestive plasmocytoma beyond the scope of its established indications.

- G20 –

SALVAGE ESOPHAGEAL ESD FOR RECURRENCE OF SUPERFICIAL CARCINOMA ON A ESD SCAR: AN ANATOMICAL LESSON OF THE MICROANATOMY OF ESOPHAGEAL RE-EPITHELIALISATION. F. Charara (1), P. Eisendrath (2), L. Verset (3), P. Demetter (3), A. Lemmers (2) / [1] Erasme Hospital, Brussels, Belgium, Upper GI surgery, [2] Erasme Hospital, Brussels, Belgium, Gastro-enterology, [3] Institut Jules Bordet, Brussels, Belgium, Histopathology.

Case Report: A 69-year-old male, in a poor general condition, presented with a 30% circumferential bulging esophageal suspicious lesion surrounded by a large flat dysplastic lesion on a long (C11M12) Barrett esophagus. Seeing its morphology, an EUS was performed with uT1bN0 staging. A thoraco-abdominal CT scan excluded any metastatic disseminations. Patient was unfit for surgery due to severe lung dysfunction, denutrition and psychiatric disorders. After multidisciplinary concertation, a staging ESD was proposed and consisted in “en bloc” resection of the whole suspicious lesion including surrounding dysplastic area. Pathological analysis of the 72 x 52mm ESD specimen revealed a 36x30mm poorly differentiated adenocarcinoma, infiltrating the submucosa on 317 micrometers depth with no lymphovascular infiltration nor perineural invasion and surrounded by high grade dysplasia. Horizontal and vertical margins were free of dysplasia, with 724 micrometers of vertical free margin. This R0 resection was classified pT1bsm1 Although not reaching curative criteria (sm1, poorly differentiated), considering the patient clinical condition, a watchful waiting strategy was adopted with the plan of further residual Barrett esophagus ablation. An FDG-PET scan 1 month after the procedure excluded any abnormal hypermetabolic activity, a thoraco-abdominal CT scan in follow up at 3 month was also negative. EUS at 4 months did not detect any extraluminal recurrence but a small nodule of 7 mm was noted in the middle of the ESD scar. Its biopsy revealed a foci of adenocarcinoma. Furthermore, biopsies obtained using the Seatlle protocol identified multiple foci of HGD on the residual Barrett. A new multidisciplinary discussion was organized and the patient again recused from surgery. Therefore, a salvage endoscopic resection of the carcinoma recurrence on the ESD scar was attempted using ESD technique. Briefly, using a HQ-190 and a 25G needle, under saline immersion conditions, a lifting was obtained by glycerol injection. The dissection was performed using Txi enhancement using a Dual Knife-J (Olympus). Fibrosis was present in the deep mucosa, but a millimetric plane of resection was found between the proper muscular layer and the lesion. Slow and cautious dissection was possible to achieve “en-bloc” complete dissection without any perforation in 55 minutes. Surprisingly, the pathological report revealed a R0 resection of a mucosal moderately differentiated 6 x 5mm adenocarcinoma with no lymphovascular infiltration, classified pT1am3 (free vertical margin of 702 micrometers). One month later, Barrett ablation program was started using RFA. At last endoscopic control, before second RFA session, residual Barrett was classified C0M1 with some small islands, with no residual dysplasia detected by biopsies. PetCt at one year of the first ESD did not revealed any local or systemic recurrence. Two questions arise from this case. Firstly, how to explain a carcinoma recurrence on a R0 resection scar without lymphovascular infiltration? Revising the slides did not give the answer. Carcinoma cell seeding during the procedure might be an issue. Observations arise from the histopathological slides illustrates that healing process after esophageal ESD might be associated to rapid mucosal resurfacing and a slower tiny fibrotic submucosal regrowth. However, this millimetric neosubmucosal layer allows to find a plane for lifting and further dissection alongside the muscle layer if needed. Although technically challenging, this procedure seems to be reasonable in expert hands and might help some patients.

- G21 -

THE CASE OF A SCRUTINIZED UNUSUAL DUODENAL TUMOR. M. Poiraud (1), F. Moulart (2), L. Verset (3), A. Lemmers (1), P. Eisendrath (2) / [1] Erasme Hospital, Brussels, Belgium, Gastroenterology Hepatopancreatology and Digestive Oncology, [2] Saint-Pierre University Hospital Center, Université Libre de Bruxelles (ULB), Brussels, Belgium, Hepato-gastro-enterology, [3] Institut Jules Bordet, Brussels, Belgium, Pathological Anatomy.

Case Report: Prediction of subepithelial lesions (SEL) based on classical endoscopic appearance is often difficult. EUS offers traditionally the advantage to characterize echogenic pattern and layers from where the lesion originates, giving information to help making a diagnosis. Further tissue sampling by EUS-FNB or mucosal-incision assisted biopsy is proposed for >20mm lesions in case of high-risk stigmata before surgical or oncological treatment. For small (<20mm) gastric SEL, with unknown histology after previous diagnosis attempt, diagnostic endoscopic resection is considered as an option. For duodenal SEL, there is no data supporting surveillance only, so efforts must be made to obtain the diagnosis. We report a case of duodenal SEL where the pathological examination of the endoscopic resection revealed the real diagnosis. A 58-year –old male underwent an esogastroduodenoscopy for gastroesophageal reflux complaints. Surprisingly, a subepithelial duodenal lesion was detected in the upper part of the second portion of the duodenum. The Paris O-Is lesion seems implanted on a large base, 2 cm proximal from the major papilla. The duodenal mucosa was considered as normal. Endoscopic ultrasound examination showed a 19x11mm well-delineated lesion originating from the submucosa, highly vascularized, with dominant hypoechogenic but heterogenic pattern. No local nor regional lymphadenopathy was observed. Based on endoscopic appearance, our first differential diagnosis hypothesis was atypical lipoma or accessory pancreas. Seeing the uncertainty of diagnosis, bite-on-bite biopsies were performed, revealing a mesenchymal cell proliferation, without mitosis. The immunohistochemical coloration showed intense anti-S100 and anti-synaptophysin positivity so as a diffuse but low anti-calreticulin signal, in favor of a granular cell tumor or Abrikosoff’s tumor. Knowing of the low but persistent risk of malignant transformation of granular cell tumor, it was decided to propose an endoscopic resection of the tumor. We attempted the removal of the lesion by ESD. Under general anesthesia, using a GIF-HQ190 gastroscope and a Dual-Knife-J (Olympus), marking dots were placed around the large implantation base. After lifting using glycerol, the lesion was carefully dissected with a safety margin from the muscular wall under near focus and under saline immersion condition for half of the lesion. Despite instability due to proximal duodenal location, the resection was completed en-bloc without any wall injury or severe bleeding. No immediate complication occurred and the patient was discharged the following day under PPI therapy. Precise diagnosis of the tumor was made by histopathology, which revealed a gangliocytic paraganglioma (GP), based on the typical presence of the three cell types: large epithelioid cells, spindle cells and ganglion cells, confirmed by immunohistochemistry positive for anti-keratin AE1/AE3, anti-chromogranin, anti-synaptophysin, anti-SNE, anti-S100 and anti-calretinin. The mitosis rate was very low with anti-Ki67 inferior to 2%. A review of the literature showed that GPs are most commonly localized in the periampullary region. Whereas the key of the diagnosis is histopathology, several authors report that the diagnosis by using preinterventional biopsies is difficult. In 84% the reported GPs were benign histologically. Those presenting with metastasis were mainly in the lymph nodes, but a few cases were reported in the liver and the bone. GPs should be considered as tumors with malignant potential. Currently no predictive markers nor histopathological patterns were identified to predict benign or aggressive behavior. Furthermore, long-term follow-up is suggested. In our case, ESD allowed an extended histopathological examination which disproved the preoperative diagnosis. Although risky and technically challenging in the duodenum, ESD appears in referral centers as a minimal invasive and good indication for further histopathological confirmation as well as a curative strategy in case of selected localized duodenal tumors. Additional material: video of the resection by ESD.

- G22 –

ENDOSCOPIC MANAGEMENT OF COLORECTAL ANASTOMOTIC LEAKAGE COMPLICATED WITH PELVIC ABSCESS: NEW STRATEGY? (WITH VIDEO). L. Monino (1), T. Moreels (1), D. Leonard (2), A. Kartheuser (2), S. Berdah (3), M. Barthet (4), J. Gonzalez (4) / [1] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, Gastroenterology, [2] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, Digestive surgery, [3] Assistance Publique des hôpitaux de Marseille, Hôpital Nord, Marseille, France, Digestive surgery, [4] Assistance Publique des hôpitaux de Marseille, Hôpital Nord, Marseille, France, Gastroenterology.

Introduction: The rate of adverse events after colorectal surgery reported in the literature is up to 20 %. The main adverse events are surgical site infection (2 to 25 %) and anastomotic leakage (2.9-15.3%). Classical management consists of (surgical or radiological) drainage of the collection and challenging redo surgery. Endoscopic guided vacuum-therapy (EVT) is a less invasive method to treat colorectal leakage with or without pelvic abscess. EVT is based on the local application of negative pressure on tissues in order to drain pus and favor granulation tissue. The success rate of this therapy in the literature is around 70-80% for closure of collections and/or anastomotic leaks. Despite the good outcome results, EVT seems to be an under-used technique. One of the reasons might be the need for multiple EVT sessions to exchange the device in order to obtain complete closure of the leak, which can be considered time-consuming and laborious. We report the case of a patient with colorectal anastomotic leakage complicated with presacral abscess successfully treated with EVT.
Case report: A 56-year old woman underwent laparoscopic anterior resection of the rectum with lymph node dissection and colorectal anastomosis for a ycT3N1 classified adenocarcinoma of the rectum in a peripheral hospital. One month later, she presented with an anastomotic leakage complicated with a presacral abscess and a rectovaginal fistula. The size of the presacral abscess was 83*75 mm. The initial treatment of this serious adverse event was the surgical placement of a transanal drain and iv antibiotics. The patient was then referred to our university hospital for definite treatment (video).

Results: Endoscopic assessment was performed under general anesthesia with fluoroscopy, and demonstrated a 2/3 circumferential dehiscence of the colorectal anastomosis with communication to a complex pelvic collection and a rectovaginal fistula. The multiloculated pelvic collection was drained endoscopically by placing double pigtail stents. At the end of the procedure, an EndoSponge (B. Braun, Melsungen AG, Tuttlingen, Germany) was placed into the lumen of the collection. The endosponge was connected to an external vacuum collector (Redyrob Trans Plus bottle; B.Braun, Melsungen AG, Tuttlingen, Germany). The EndoSponge was changed endoscopically every 3 to 4 days under general anesthesia, with a fluoroscopic evaluation of the collection size every other EndoSponge replacement procedure. After 2 weeks, the double pigtail stents were removed. At day 19, the recto-vaginal fistula was completely closed. At day 26, the 8th EndoSponge was placed and the leakage with the adjacent collection were also completely closed. Two months later, CT-Scan showed no recurrence of the pelvic collection and no recto-vaginal fistula. Endoscopic and radiologic control at 9 months showed a normal colorectal anastomosis without recurrence of pelvic collection or recto-vaginal fistula. The management of adverse events after colorectal surgery is challenging and requires a multi-disciplinary approach. The combined experience of two university centers with expertise in the management of surgical anastomotic complications, both in the upper and lower GI tract, has led to the development of a treatment algorithm for colorectal anastomotic complications (Figure 1).
Conclusion: This case report highlights the effectiveness of EVT in the management of complex colorectal anastomotic leakage. Although multiple sessions are required, EVT is less invasive than redo surgery and is shown to be very effective in the treatment of anastomotic leakage after colorectal surgery. Future multicenter studies are needed to confirm EVT efficacy and validate the proposed algorithm.

- G23 -

ANALYSIS OF FACTORS INFLUENCING OUTCOME OF ANGIOGRAPHIC EMBOLIZATION FOR SEVERE, GASTRODUODENAL HEMORRHAGE RELATED TO PEPTIC ULCERATION. C. Vanhoenacker (1), E. Hufkens (2), I. Demedts (3), G. Maleux (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Radiology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Departement of Gastroenterology and Hepatology, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Transcatheter embolization is an established treatment option to manage severe gastroduodenal hemorrhage refractory to medical and endoscopic management. Factors potentially influencing clinical outcome are not well-studied.
Aim: To evaluate the outcome of patients who underwent a transcatheter arterial embolization (TAE) for severe, gastroduodenal hemorrhage associated with peptic ulcer and refractory to medical and endoscopic therapy; to compare the outcome of different embolic agents and to evaluate factors associated with early recurrent bleeding and 30-day mortality.
Methods: A monocenter, retrospective study of 76 consecutive patients who underwent TAE for bleeding gastroduodenal peptic ulcers from 2005-2020. Patient demographics, endoscopy findings, co-morbidities and interventional procedure findings were recorded. The outcome measures were technical and clinical success, procedure related complications, recurrent bleeding, length of hospital stay, 30-day mortality and overall survival.
Results: The technical success rate was 90.8% and the clinical success was 65,8%. The rebleeding and 30-day mortality were 30,7% and 22,4% respectively. A higher international normalized ratio (INR) was a statistically significant risk factor for 30-day mortality (OR, 7.15; 95% CI, 1.67-30.70; p=0.008). A lower Charlson Comorbidity Index (CCI) and a lower Rockall score were significantly associated with a longer overall survival (HR, 1.24; 95% CI, 1.14-1.35; p =0.0001) and (HR, 1.32; 95% CI, 1.10-1.59; p=0.003) respectively. The occurrence of early rebleeding is significantly associated with a lower overall survival (HR, 2.72; 95% CI, 1.57-4.71; p=0.0004). There were no statistically significant differences in outcome or overall survival using different embolic agents.
Conclusions: Type of embolic agent did not influence overall survival. A higher INR was a significant risk factor with a higher 30-day mortality. A lower CCI, a lower Rockall score and the absence of early rebleeding were significantly associated with a longer overall survival.

- G24 -

DIGESTIVE NEO-EPITHELIZATION AFTER ENDOSCOPIC STENTING FOR COMPLETE UPPER DIGESTIVE TRACT DISUNION. S. Ouazzani (1), A. Lemmers (1), J. Gonzalez (2), J. Closset (3), I. El Messaoui (3), J. Deviere (1), M. Barthet (2) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, [2] Assistance Publique des hôpitaux de Marseille, Hôpital Nord, Marseille, France, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, [3] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Digestive Surgery.

Introduction: Complete digestive disunion due to anastomotic leakage is a potential life-threatening complication of abdominal surgery and is considered as a total contra-indication to endoscopic repair. However, recent publications showed possibility of endoscopic treatment by insertion of SEMS.
Aim: The aim of this series is to show the possibility of endoscopic management of some selected cases with complete circumferential digestive disunion due to postoperative anastomotic leakage, all treated by endoscopic insertion of SEMS.
Methods: We reviewed, from prospective databases, patients hospitalized in two European tertiary care centers (Hôpital Nord, AP-HM, Marseille, France; Hôpital Erasme, ULB, Brussels, Belgium) for complete upper-GI anastomotic disunion between 2009 and 2020 and treated by endoscopic insertion of a SEMS. Endoscopic treatment was discussed with the surgical team and chosen in case of impossibility or failure of previous attempt of surgical repair of the anastomosis. Treatment was performed with therapeutic gastroscope (with unique large canal or double canal) under general anesthesia, on intubated patients in supine position, with CO2 insufflation and fluoroscopic guidance, after eventual surgical or percutaneous drainage. The choice of the type of stent (fully or partially covered SEMS) was left at the endoscopist discretion.
Results: A total of 7 patients (4 males; median age: 60 years old, range: 49-77) with complete digestive disunion of upper-GI tract were successfully treated by endoscopy. Three patients (43%) had a malignant disease, one of them having previous chemoradiotherapy. The first endoscopy was performed after a median of 14 days after the surgery (range: 2-30) and in 4 patients, a previous surgical or percutaneous drainage was attempted. Three patients (43%) experienced distal migration of SEMS (20% of all placed stents), without precluding the healing (one had already disunion healed, the others had SEMS replacement or repositioning). There was no hemorrhage nor perforation. All completely healed after a median of 8 weeks (range: 4-32) of stenting, needing a median of 3 endoscopic sessions (range: 2-6) with a median number of 2 SEMS insertion (range: 1-6) by patient. Six patients had a median follow-up of 38 months (range: 20-120). Among them, three patients (50%) experienced a stricture, all successively treated by endoscopic dilation (median of 3 sessions; range: 2-8). Moreover, no patient experienced recurrence of leakage or other complication.
Conclusions: This case series showed that complete digestive rupture could be, in selected cases, successively treated by endoscopy with the use of fully or partially covered metal stents, adding a proof-of-concept about a guided tissue regeneration alongside SEMS.

- G25 -

EUS-GUIDED VERSUS PTC-GUIDED RENDEZ-VOUS IN CASE OF FAILED ERCP: A CASE-CONTROL STUDY. M. Hanssens (1), H. Degroote (2), P. Hindryckx (3) / [1] Ghent University Hospital, Ghent, Belgium, Internal medicine, [2] Ghent University Hospital, Ghent, Belgium, Gastroenterology, [3] Ghent University Hospital, Ghent, Belgium, Gastroenterology.

Introduction: Endoscopic ultrasound-guided rendez-vous (EUS-RV) is a recently added alternative salvage technique to percutaneous transhepatic cholangiography rendez-vous (PTC-RV) for achieving cannulation in failed ERCP. Comparative data on these two techniques are lacking.
Aim: The aim of this study was to evaluate the efficacy and safety of EUS-RV versus PTC-RV in a tertiary referral center.
Methods: A case-control study was conducted in the tertiary referral center, Ghent University Hospital. All consecutive patients that underwent a rendez-vous procedure between February 2014 and September 2021 for failed biliary cannulation were included. Patients that underwent PTC-RV (between February 2014 and February 2018) were compared to those who underwent EUS-RV (between March 2018 and September 2021). A subanalysis was performed for malignant biliary strictures (MBO), benign biliary strictures (BBO) and common bile duct stones (CBDS). The primary endpoints of interest were technical success rate and complication rate. These outcome variables were compared among techniques using Fisher's exact test. Statistical analyses were performed using STATA version 15.
Results: A total of 55 patients were included in this study; 19 (34.5%) underwent PTC-RV; the remaining 36 (65.4%) patients underwent EUS-RV. Demographics for both cohorts are shown in table 1. Of the PTC-RV procedures, 18/19 (94.7%) were technically successful, as compared to 28/36 EUS-RV procedures (77.8%) (p = 0.141; fig. 1). Adverse events were reported in 6/19 patients (31.6%) that underwent PTC-RV and in 10/36 patients (27.8%) that underwent EUS-RV (p= 0.765; fig. 2). Major adverse events (i.e. requiring endoscopic or percutaneous, reinterventions, surgery or intensive care admission) were seen in 4/19 (21.1%) and 2/36 (5.6%) of the PTC-RV and EUS-RV procedures, respectively (p< 0.001).
Conclusions: In our cohort, EUS-RV had an acceptable success rate and was associated with less serious adverse events as compared to PTC-RV.

- G26 -

LUMEN-APPOSING METAL STENTS FOR THE TREATMENT OF SHORT REFRACTORY GASTROINTESTINAL STRICTURES: A PRELIMINARY EXPERIENCE. P. Hindryckx (1), H. Degroote (2) / [1] Ghent University Hospital, Ghent, Belgium, Gastroenterology, [2] Ghent University Hospital, Ghent, Belgium, Gastroenterology.

Introduction: Some short gastrointestinal (GI) strictures (such as anastomotic strictures) can be quite refractory to dilatation. Stenting with regular esophageal stents is associated with stent-related adverse events such as stent migration, inflammatory reactions, new stricture formation, etc… Lumen-apposing metal stents (LAMS) are light and ultrashort fully covered stents with broad flanges, offering the theoretical advantage of reduced migration risk and less stent-related adverse events.
Aim: We investigated the potential use of LAMS in the management of short refractory strictures in a small cohort of patients
Methods: We retrospectively reviewed the medical records of patients that underwent stenting with a LAMS for short refractory GI strictures. Outcomes of interest were technical success rate, adverse event rate (including stent migration) and stricture resolution.
Results: Seven patients with severe short refractory GI strictures underwent stenting with a LAMS. In 3 of them, the stricture was at the level of a surgical anastomosis. Technical success rate was 100%. In one patient with a very high esophageal stricture, the stent was removed after two days because of local complaints. In 2/7 patients (28.7%), stent migration was seen. No other stent-related adverse events were noted. Successful medium-term resolution (follow-up range 2-7 months) was obtained in 3/7 patients (42.9%). In 1 patient, the stenosis came back only 1 week after removal of the LAMS. Importantly LAMS placement did not lead to new stricture formation or extension of the treated stricture.
Conclusions: LAMS can be considered for the treatment of short refractory GI strictures. Although the technical success rate is 100%, the clinical success rate on the medium term remains disappointing and the risk of migration can not be eliminated.

- G27 -

ENDOSCOPIC EXPLORATION OF THE EXCLUDED STOMACH IN PATIENTS WITH ROUX-EN-Y GASTRIC BYPASS: COMPARISON OF SINGLE-BALLOON AND MOTORIZED SPIRAL ENTEROSCOPY. T. Moreels (1), L. Monino (1), P. Deprez (1), H. Piessevaux (1) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Hepato-Gastroenterology.

Introduction: The motorized spiral enteroscope (MSE) is a newly designed enteroscope with a motorized spiral overtube allowing deep and even complete enteroscopy in patients with normal anatomy. Surgically altered anatomy was initially considered a contraindication for the use of MSE. Therefor little information is available on the feasibility and safety of MSE in patients with Roux-en-Y gastric bypass. No comparative studies of the efficacy of MSE in comparison with single-balloon enteroscopy (SBE) are available.
Aim: To compare feasibility and safety of MSE and SBE to explore the excluded stomach in patients with Roux-en-Y gastric bypass.
Methods: Data of all Roux-en-Y gastric bypass patients who were referred for endoscopic exploration of the excluded stomach during 2020-2021 were collected and analysed: age, sex, enteroscope used, procedure time, technical success, endoscopic intervention and adverse events. All enteroscopies were performed under fluoroscopic control, allowing visual comparison of insertion depth. MSE was performed with the PSF-1 enteroscope, SBE was performed with the SIF-Q180 or the XSIF-180JY enteroscope.
Results: In 2 years time, a total of 18 patients underwent enteroscopy using either SBE (n=9) or MSE (n=9) to explore the excluded stomach. The male/female ratio was 7/11 with a mean age of 57±3 years in the MSE group and 51±3 years in the SBE group (p=0.37, Student's t test). The excluded stomach was successfully intubated in 6/9 (67%) using MSE and in 7/9 (78%) using SBE (p=0.60, Chi-square test) with comparable total procedure times: 53±8 min (range 29-84) for MSE vs 61±13 min (range 30-121) for SBE (p=0.62, Student's t test). However, in the 2 failed SBE cases, the pylorus was reached without intubation of the excluded stomach, whereas in the 3 failed MSE cases, the pylorus was reached in only 1, and in the 2 other failures, MSE did not even reach the Roux-en-Y anastomosis. No adverse events occurred in either group, apart from 1 case of superficial mucosal lacerations at the upper oesophageal sphincter in the MSE group. Endoscopic findings in the excluded gastrointestinal segments included diversion gastritis, gastric and duodenal ulcers, pyloric hypertrophy, duodenal polyp, duodenal angioma and anastomotic ulcers. Enteroscopic interventions included hemostatic clipping, argon plasma coagulation, polypectomy and mucosal biopsies. In 4 patients (31% of successful procedures) endoscopic findings were normal.
Conclusions: Endoscopic exploration of the excluded stomach is challenging in patients with Roux-en-Y gastric bypass. Preliminary analysis of a cohort of 18 patients showed that MSE and SBE have comparable success rates and total procedure times without serious adverse events, with positive findings in the majority of the patients. However, whereas SBE reached the pylorus in 2 failed procedures, MSE failed before reaching the Roux-en-Y anastomosis. Enlarging the cohort is necessary to fully evaluate the efficacy and safety of MSE in patients with surgically altered anatomy.

- G28 -

FIRST DATA OF BOTOMY TRAIL: DESCRIPTIVE INTERIM RESULTS ON CLINICAL EFFICACY OF INTRAPLYORIC BOTULINUM TOXINE INJECTION AND G-POEM IN REFRACTORY GASTROPARESIS. P. Corens (1), S. Bouhadan (2), H. De Schepper (2), P. Dewint (3) / [1] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology, [2] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology and Hepatology, [3] Maria Middelares Ziekenhuis, Gent, Belgium, Gastroenterology.

Introduction: Gastroparesis is a chronic motility disorder characterized by delayed gastric emptying in the absence of mechanical obstruction. In patients with refractory gastroparesis, therapeutic management is challenging. To date, several interventional endoscopic therapies have been described, all targeting the pyloric sphincter. These include intrapyloric injection of botulinum toxin (botox) and Gastric peroral endoscopic myotomy (G-POEM).
Aim: To evaluate clinical efficacy of botox and G-POEM in patients with refractory gastroparesis.
Methods: A multi-center, observational, prospective trial was performed wherein patients with refractory gastroparesis were included in a single-arm treatment group. Gastric emptying was evaluated with (13)C-octanoate breath or scintigraphy test at baseline, after botox and G-POEM, with a total follow-up of 12 months. Patients underwent endoscopic treatment with botox 4x25U and G-POEM in a consecutive order with a minimal interval of 4 weeks between both procedures, with G-POEM only in patients with ongoing symptoms or after relapse of symptoms. Clinical response was evaluated with the Gastroparesis Cardinal Symptom Index - Daily Diary (GCSI-DD) at baseline, 4 weeks after botox and 3, 6 and 12 months after G-POEM. In patients who initially responded to botox, additional symptom evaluation was performed when clinical relapse occurred. Clinical success was defined as a decrease of 1 point in the mean total GCSI-DD score. We report the interim results of patients with a minimum follow-up duration of 3 months after G-POEM.
Results: Ten patients (4 male; age 22-74 mean 49 - 17) with idiopathic (n=7), post-surgical (n=2) or diabetic gastroparesis (n=1) were included, with a follow-up of respectively 10; 9 and 4 patients at 3; 6 and 12 months after G-POEM. Botox resulted in clinical success in 50% of patients (5/10), albeit with relapse of symptoms in all patients after a median time of 10 weeks. G-POEM resulted in clinical success in 70% (7/10), 66% (6/9) and 75% (3/4) of patients at 3 months, 6 months and 1 year respectively. Compared to baseline, botox resulted in an improvement of symptom score, although not significant [mean GCSI-DD 3.15 +/- 1.04 to 2.37 +/- 1.17; p = .058]. G-POEM resulted in significant improvement of symptom score at 3 months [mean GCSI-DD 2.68 +/- 1.00 vs. 1.36 +/- 1.34; p 0.024], at 6 months [mean GCSI-DD 2.67 +/- 1.06 vs. 1.31 +/- 1.36; p 0.030] but not after 12 months [mean GCSI-DD 2.38 +/- 1.08 vs. 1.01 +/- 0.89; p 0.174]. Gastric emptying did not improve significantly after botox [mean T1/2 157.33 +/- 28.28 to 125.50 +/- 64.89; p = .297] or G-POEM [mean T1/2 134.25 +/- 80.44 to 113.50 +/- 34.67; p =.650]. Technical success was achieved in 100% of cases. Two delayed gastric perforations occurred at day 4 and 5 after G-POEM respectively, which necessitated antibiotic treatment and urgent surgical laparoscopic intervention.
Conclusions: In this interim analysis, clinical success of botox was 50%, albeit with relapse of symptoms in all patients after a median time of 10 months. In comparison with botox, G-POEM seems more efficacious, with a clinical success rate of up to 75% at month 12.

- G29 -

SHORT DOUBLE BALLOON ENTEROSCOPY ASSISTED ENDOSCOPIC RETROGRADE CHOLANGIO-PANCREATOGRAPHY IN PATIENTS WITH SURGICALLY ALTERED ANATOMY. R. Wadhwa (1), A. Ravindranath (2) / [1] Apollo BGS Hospital, Mysore, India, Gastroenterology, [2] Apollo BGS Hospital, Mysore, India, Pediatric Gastroenterology.

Introduction: Double balloon enteroscopy assisted endoscopic retrograde cholangiopancreatography (DBE-ERCP) is performed where endoscopic access to biliary system becomes formidable due to surgical alteration of anatomy. Short DBE has the added advantage of greater stability and maneuverability compared to long DBE. Moreover, standard ERCP accessories can be used. We present a single center experience of short DBE-ERCP.
Aim: The aim of this study was to ascertain the technical and clinical success of using Short DBE-ERCP scope in patients with surgically altered anatomy.
Methods: Records of all patients who underwent short DBE-ERCP were retrieved. Baseline characteristics and details about the surgery were collected. Details of the procedure, time taken and complications, if any, were noted. Clinical and biochemical data on follow-up were assessed. Endoscopic success, diagnostic success, therapeutic success and clinical success were evaluated.
Results: Eight patients underwent 12 sessions of short DBE-ERCP over a period of 3 years. Roux-en-Y anatomy was present in 7/8 and Billroth II anatomy in 1/8. Indications were: benign stricture at hepaticojejunostomy site in 3, choledocholithiasis in 1, cholangiocarcinoma of common bile duct 3 and cholangiocarcinoma at hepaticojejunostomy site in 1. Endoscopic success was attained in 10/12 (83.3%), diagnostic success in 10/10 (100%) and therapeutic success in 9/10 (90%). Clinical success was achieved in 7/8 (87%) patients. Self-expanding metal stents were placed in 4, plastic stents in 2, balloon dilatation of stricture was performed in 1. Percutaneous transhepatic biliary drain (PTBD) assisted cannulation was performed in 2 patients.
Conclusions: Short DBE-ERCP can achieve technical success in the majority. PTBD assisted cannulation can be achieved in selected cases. Ability to use standard ERCP accessories and greater stability compared to long enteroscopes and colonoscopes are specific advantages.

BELGIAN HELICOBACTER AND MICROBIOTA STUDY GROUP

- H01 -

GASTRIC NON-HELICOBACTER PYLORI HELICOBACTER SPECIES (NHPH) AND DISEASE: FROM ANIMALS TO CLINICAL RELEVANCE IN HUMANS. E. Taillieu (1), S. Rutten (2), S. Michiels (2), Y. Arnst (2), S. De Bruyckere (1), K. Chiers (1), F. Van Aert (2), H. De Schepper (2), E. Callewaert (3), C. George (3), W. Van Moerkercke (3), G. Vanneste (4), N. Van Heddegem (5), E. Vanderstraeten (5), F. Haesebrouck (1), C. Van Steenkiste (5) / [1] Ghent University, Ghent, Belgium, Faculty of Veterinary Medicine, Department of Pathobiology, Pharmacology and Zoological Medicine, [2] University Hospital Antwerp, Edegem, Belgium, Department of Gastroenterology and Hepatology, [3] AZ Groeninge, Kortrijk, Belgium, Department of Gastroenterology and Hepatology, [4] AZ Groeninge, Kortrijk, Belgium, Department of Pathological Anatomy, [5] AZ Maria Middelares, Ghent, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Helicobacter (H.) pylori is a well-known microorganism that colonizes the human stomach, with a global prevalence of more than 50%; infection can cause mainly gastritis and peptic ulcer disease, but also gastric carcinoma and gastric mucosa-associated lymphoid tissue (MALT) lymphoma. Since the discovery of H. pylori, various gastric non-Helicobacter pylori Helicobacter species (NHPH) have been identified which naturally colonize the stomach of their corresponding animal host, including pigs, cats and dogs. Several of these have also been detected in human patients suffering from gastric complaints, admittedly at a much lower prevalence (0.2-6.0%), proving their zoonotic potential. Cases of gastric NHPH infection have already been associated with chronic gastritis, peptic and duodenal ulcer disease, and low-grade gastric MALT lymphoma, with a higher risk of developing gastric MALT lymphoma than with H. pylori.
Aim: This is the first study to determine the clinical relevance of several possibly zoonotically important pig-, cat- and dog-associated gastric NHPH in large, well-defined patient populations at risk in a systematic manner.
Methods: Gastric biopsy samples were collected in both a retrospective (from 2014 to 2020) and prospective (started January 2020 and is ongoing) manner. Patients with the following diagnoses were included: chronic gastritis or presence of lymphoid aggregates/follicles (CG), peptic ulcer disease (PU), and MALT lymphoma. Exclusion criteria were pregnancy, age <18 years, previous diagnosis of H. pylori infection and current or recent (i.e. <4 weeks) NSAID intake. Prospectively included patients received a survey in order to collect information about medication use, animal contact, meat consumption and ethnicity. In the lab, DNA was extracted from each patient sample. A Helicobacter genus-specific PCR assay was performed as well as species-specific PCR assays, followed by sequencing of amplicons positive in at least one assay, in order to determine and specify the possible presence of the pig-associated H. suis and cat-/dog-associated H. felis, H. bizzozeronii, H. salomonis, H. heilmannii and H. ailurogastricus. Prospectively included patients positive for gastric NHPH infection were administered triple eradication treatment. Clinical remission was checked within 8 to 10 weeks post-treatment.
Results: In total, 426 patients (mean age: 61 years; M/F: 0.46; CG/PU/MALT lymphoma: 361 (84.7%)/55 (12.9%)/10 (2.3%)) were included retrospectively. Epigastric pain was the most common complaint at anamnesis (28.4%). By means of PCR and sequencing, gastric NHPH were detected in 113 patients (26.5%), with the most prevalent species being H. bizzozeronii (40/113; 35.4%), followed by H. felis (39/113; 34.5%), H. suis (14/113; 12.4%) and H. salomonis (3/113; 2.7%). Infections with more than one gastric NHPH were detected in 15 patients (13.3%). In 2 patients (1.8%), infection with a gastric NHPH from the group of cat-/dog associated species was detected by sequencing of the amplicon obtained in the genus-specific PCR assay. As this is based on the 16S rRNA gene which is identical for all species within this group of NHPH (formerly H. heilmannii type 2), these could not be further specified. Prevalence was highest in patients with PU (17/55; 30.9%), followed by CG (95/361; 26.3%) and MALT lymphoma (1/10; 10%). Up until now, 32 patients were included prospectively (mean age: 55 years; M/F ratio: 0.53; CG/PU/MALT lymphoma: 23 (71.9%)/6 (18.8%)/3 (9.4%)). Currently, gastric NHPH were detected in gastric biopsies of 11 patients (34.4%), including 6 infections with H. bizzozeronii (54.5%), 4 with H. felis (36.4%) and 1 with H. salomonis (9.1%). No statistically significant associations were found between the presence of gastric NHPH infection and sociodemographic factors, including use of proton pump inhibitors, contact with animals, consumption of meat and ethnicity. Clinical remission was reported in 2 out of 2 patients who received triple eradication treatment.
Conclusions: In these populations at risk, prevalence of gastric NHPH is much higher than would be expected from existing literature. Furthermore, in contrast to existing literature, H. bizzozeronii and H. felis show a higher prevalence than H. suis. These results suggest that patients presenting with gastric complaints should not only be referred for gastric biopsy in order to perform routine testing for H. pylori, but also for detection of zoonotically important gastric NHPH by PCR. Preliminary remission results of our ongoing study are promising and further confirm the relation between gastric NHPH infection and gastric pathology.

- H02 -

DIFFERENCES IN MANAGEMENT OF HELICOBACTER PYLORI INFECTION: AN OBSERVATIONAL STUDY. G. Rasschaert (1), R. Ntounda (2) / [1] Universitair Ziekenhuis Brussel, Brussels, Belgium, Gastroenterology and Hepatology department, [2] CHU Saint-Pierre, Brussels, Belgium, Gastroenterology and Hepatology department.

Introduction: Despite multiple recommendations, management of Helicobacter pylori (Hp) infection and eradication rates remain highly variable across countries and sometimes within the same region.
Aim: Obtain insight in physicians management of Hp infection, through a questionnaire, as compared to existing guidelines.
Methods: Our questionnaire, based on the international recommendations on the management of Hp infection (Maastricht V/Florence Consensus), was submitted anonymously to two major scientific associations of physicians: mainly Belgian (both French-speaking and Dutch-speaking) and African (French-speaking).
Results: 138 practitioners responded to the questionnaire, including 95 in the Belgian group and 43 in the African group. The Belgian group has two subgroups: Dutch-speaking (60) and French-speaking (35). Throughout thirty questions studied, the difference between the Belgian and African group is observed only in the use of non-invasive tests ($p=0.013$), in eradication control ($p=0.004$) and in the search for Hp infection before bariatric surgery ($p<0.05$). On the one hand, there is no significant difference in the two Belgian linguistic subgroups. Only 55.8% is interested in therapeutic success rate. On the other hand, only 31.9% of practitioners have an overall therapeutic success > 80%. In addition, overall scores on knowledge of recommendations are often questionable.
Conclusions: There are no significant discrepancies in the management of Hp infection between Belgian and African practitioners despite the difference in diagnostic and therapeutic means. There is an important gap in several aspects between international recommendations and daily practice. Considerable effort in popularizing the guidelines seems to be useful.

- I01 -

ENDOSCOPIC OUTCOME IN TOFACINITIB TREATED PATIENTS CORRELATED WITH TOFACITINIB TISSUE EXPOSURE. B. Verstockt (1), D. Alsoud (2), J. Van Oostrom (3), J. Smith (4), J. Stylli (4), S. Singh (4), S. Van Gennep (3), P. Rahimian (4), J. Sabino (1), M. Ferrante (1), S. Singh (4), G. D'haens (3), S. Vermeire (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Chronic Diseases and Metabolism, [3] Amsterdam UMC, Amsterdam, The Netherlands, Department of Gastroenterology and Hepatology, [4] Progenity, San Diego, United States, Progenity.

Introduction: Small molecules are being added to the treatment armamentarium of ulcerative colitis (UC). In contrast to monoclonal antibodies, very little is known about their pharmacokinetic-pharmacodynamic profile.
Aim: To assess pharmacokinetic-pharmacodynamic changes in Tofacitinib (TFC) treated UC patients, with a focus on STAT3 phosphorylation as it has been proposed as a marker of efficacy.
Methods: Thirty UC patients initiating TFC therapy 10mg BID were prospectively monitored. At week 8, patients could de-escalate to 5mg BID or maintain 10mg BID depending on their response. Endoscopic assessment and sampling (colonic tissue and serum) was performed at baseline and 8-16 weeks after TFC initiation. Endoscopic improvement was defined as Mayo endoscopic subscore 0-1. TFC was extracted from tissue using acetonitrile, dried down and quantitated using mass spectrometry. Both total as well as phosphorylated STAT3 were measured in lysed tissue using specific antibodies with an ultrasensitive luminescent oxygen channelling assay.
Results: TFC tissue and serum concentrations correlated significantly ($r=0.92$, $p<0.001$), though were significantly higher in tissue (median 520.19ng/g vs 17.35ng/mL, $p<0.001$). In contrast to TFC serum exposure ($p=0.26$), TFC tissue exposure at the end of induction was associated with endoscopic improvement by week 16 ($p=0.04$). In TFC responders (n=14), TFC tissue exposure exceeded the concentration required to block 90% of the target (IC90) reported in literature (median tissue exposure 1,055.00ng/g; IC90 823ng/g). TFC tissue exposure in non-responders (n=16) was lower, but clearly exceeded the IC50. Although IL-6 was not significantly downregulated after TFC induction, a significant decrease in the ratio of mucosal IL-6 driven phosphorylated STAT3 over total STAT3 (pSTAT3/STAT3) was observed in responders ($p=0.05$), but not in non-responders ($p=0.88$). The pSTAT3/STAT3 ratio also correlated significantly with faecal calprotectin ($r=0.35$, $p=0.05$), but only weakly with the Mayo endoscopic sub score ($r=0.22$, $p=0.13$). Baseline mucosal pSTAT3/STAT3 did not differ significantly between future responders and non-responders.
Conclusions: We could demonstrate for the first time a mucosal exposure-response relationship with TFC in UC patients. Additionally, pSTAT3/STAT3 ratio was identified as potential molecular marker to track response directly linked to the mode-of-action of TFC. Whether an increased local dose of TFC could result in better efficacy without compromising safety should be further explored.

- I02 -

REMISSION STATE IN INFLAMMATORY BOWEL DISEASE PATIENTS ON ANTI TNF OR VEDOLIZUMAB: A CONFOCAL ENDOMICROSCOPY STUDY. J. Loly (1), S. Vieujean (1), C. Reenaers (1), C. Van Kemseke (1), L. Seidel (2), J. Somja (3), E. Louis (1) / [1] CHU Liege, Liège, Belgium, Gastroenterology, [2] CHU Liege, Liège, Belgium, Biostatistics, [3] CHU Liege, Liège, Belgium, Pathology.

Introduction: Confocal endomicroscopy is a technique allowing the in vivo assessment of the superficial layers of the mucosa, including the epithelium, the surrounding connective tissue and blood vessels. Some of the features observed by endomicroscopy can't be assessed by classical histology. Preliminary studies have already suggested its added value in the assessment of endoscopic remission in IBD. However, most of these studies were performed on patients still having some endoscopic activity. Furthermore, to our knowledge, no study has used endomicroscopy to compare the state of remission in IBD patients under vedolizumab and anti TNF.
Aim: Our aim was to disclose persisting endomicroscopy anomalies in patients with full endoscopic healing and to compare them between vedolizumab and anti-TNF.
Methods: we screened patients with CD or UC treated for more than 6 months by adalimumab, infliximab, or vedolizumab, and being in steroid-free clinical (PRO2) and biological remission (CRP<5 mg/l and F Cal <250 microg/g). Confocal endomicroscopy analysis was performed in the ileum, right colon, transverse colon, left colon and rectum. In each ileal segment, we recorded fluorescein leakage, the presence of epithelial erosions, gap junction anomalies and vessel diameter. In each colonic segment, we recorded the presence of fluorescein leakage, crypt dilatation, vessel diameter, and hypervascularization. Patients were prospectively follow-up and clinical relapses (PRO2 + one objective marker) were recorded.
Results: 72 CD and UC patients treated by biologic therapy and in clinical remission were screened. 37 of them were also in endoscopic remission (eMayo=0 in UC and absence of ulcer or erosion in CD) and were included in our study. Their treatment was infliximab (n=5), adalimumab (n=16), vedolizumab (n=15) and ustekinumab (n=1). We found a persistence of residual endomicroscopy anomalies in the different segments in a substantial number of patients (fluorescein leakage in 89% of ileum segment, 50% of right colon, 57% of transverse colon, 36% of left colon, 30% of rectum; crypt dilatation in 61% of right colon, 59% of transverse colon , 57% of left colon, 70% of rectum; Erosion in 38% of ileum, Gap junction in 70% of ileum, vessel dilatation in 84% of ileum segment, 82% of right colon, 61% of transverse colon, 76% of left colon, 62% of rectum; hypervascularisation in 28% of ileum segment, 44% of right colon, 40% of transverse colon, 40% of left colon, 32% of rectum). These persisting abnormalities were not significantly associated with any demographic or clinical characteristics including the treatment (anti-TNF or vedolizumab), nor with histologic parameters (almost all patients were in histologic remission), levels of CRP or Fecal Calprotectin. The average follow-up time was 33.4 (+/- 9.5) months. Among the 37 patients, 7 (18.9%) relapsed. The risk of relapse was not associated with any clinical, biological, histologic or endomicroscopy factor.
Conclusions: Despite endoscopic, biological and even histologic remission, we found a high prevalence of endomicroscopic abnormalities, which were not different between anti-TNF and vedolizumab treated patients. The clinical significance of these anomalies remains to be clarified.

- I03 -

BIOLOGICAL THERAPIES AND SMALL MOLECULES ARE EFFICACIOUS IN PATIENTS WITH MODERATE-TO-SEVERE ULCERATIVE PROCTITIS. P. Lemmens (1), J. Sabino (1), E. Dubois (1), B. Verstockt (1), S. Vermeire (1), M. Ferrante (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Departement of Gastroenterology and Hepatology.

Introduction: Although adalimumab (ADM), golimumab (GOL), infliximab (IFX), tofacitinib (TFC), ustekinumab (UST) and vedolizumab (VDZ) have been shown efficacious for the treatment of moderate-to-severe ulcerative colitis (UC), data on treatment of patients with ulcerative proctitis (UP, inflammation up to 15cm from the anal verge) are scarce.
Aim: We aimed to evaluate the effect of biologicals (ADM, GOL, IFX, UST, VDZ) and small molecules (TFC) on active UP.
Methods: We conducted a retrospective study in which we included 74 patients (median age at induction 41 (IQR 32-52) years) with active UP (Mayo endoscopy sub-score of $\geq$2) initiating a biological therapy (ADM, GOL, IFX, UST, and VDZ) or small molecule (TFC) in our tertiary referral centre between 02-2005 and 02-2021. The primary endpoint was steroid-free clinical remission at week 20 without prior need for dose optimization. Clinical remission was defined as a total Mayo score $\leq$2 with no individual sub-score >1. We also evaluated clinical response at short-term follow up (FU). Clinical response was defined as a decrease from baseline in the total Mayo score $\geq$3 and $\geq$30%, plus a decrease in the rectal bleeding sub-score of $\geq$1 point, or an absolute rectal bleeding sub-score $\leq$1. In addition, we investigated the long-term outcomes. For the latter we used the adapted Mayo score (sum of stool frequency subscore and rectal bleeding subscore), since colonoscopy was not routinely performed at long-term FU. We collected demographic, clinical, biochemical, endoscopic and treatment-related data.
Results: In total 74 patients (57% male) undergoing 93 courses of therapy for UP (16 ADM, 5 GOL, 19 IFX, 4 UST, 44 VDZ, 5 TFC) were included. At week 20, 31/93 (33.3%) patients achieved steroid-free clinical remission, and 48/93 (51.6%) patients achieved steroid-free clinical response, both without prior need for dose optimization. No predictors of steroid-free clinical remission could be identified. Of the 93 patients 91 had a FU under the index-therapy beyond week 20. The median duration of FU was 15.5 (IQR 3-31) months. Of the 31 patients with initial steroid-free clinical remission, 26 patients (83.8%) had sustained steroid-free clinical remission. During follow-up, 49/91 (53,8%) patients needed to discontinue their treatment, one due to non-treatment related death. Only one patient developed a serious adverse event, namely a tuberculosis infection.
Conclusions: Biological therapies and small molecules are a safe treatment for patients with UP, with an overall steroid-free clinical remission rate of 34.4% (32/93) at short-term FU. Our results are lower than in previous studies, probably because of the more stringent definitions of clinical remission and response.

- I04 -

THE DYNAMIC OF THE MOLECULAR CLASSIFICATION OF CROHN'S DISEASE. N. Seyed Tabib (1), S. Verstockt (2), B. Verstockt (3), J. Sabino (3), M. Ferrante (3), S. Vermeire (3) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Translational Research in GastroIntestinal Disorders, [2] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of chronic diseases, metabolism, and ageing, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: There is a need for a comprehensive classification system to better characterize patients with Crohn's disease (CD). It is crucial to better differentiate disease subtypes and consequently tailor treatment accordingly.

Aim: We aimed to develop scores characterizing the degree of dysbiosis and dysregulation of the immune proteome as well as the intestinal barrier integrity, autophagy, and unfolded protein response (UPR) in CD patients. We investigated the dynamic properties of these scores and their association with important clinical outcomes.
Methods: We collected faecal samples, ileum and colon biopsies, and serum samples of a total of 312 CD patients and 148 controls (CO). In 20 patients starting biological therapy, these samples were collected both at baseline and after 6 months. Intestinal microbiota (16S), intestinal epithelial cell function (RNA expression), and serum proteomics (inflammatory proteins (OLINK)) were performed on these samples. The microbiome dysbiosis index (MDI) was calculated as previously described(1). Panelised logistic regression was used as classification model for proteomics and RNA expression data, leading to inflammatory proteomic score (IPS), barrier integrity score (BIS), autophagy score (AUS), and UPR score. Patients were then divided into quartiles based on the results from Q1 (the least dysfunctional state) to Q4 (the most dysfunctional state). We correlated these scores with C-reactive protein (CRP), faecal calprotectin (FC), Montreal classification, and also with important outcomes such as the need for surgery.
Results: Both the MDI and IPS positively correlated with CRP (spearman r=0.27 and r=0.73 respectively, both p<0.0001) and FC levels (spearman r=0.3 and r=0.68 respectively, both p<0.0001). The AUS positively correlated with age at diagnosis (spearman r=0.28, p=0.0035). The UPR score and BIS showed a weak correlation with disease duration (spearman r=0.3 and r=0.21, p=0.0019 and p=0.031 respectively). Importantly, both the BIS and AUS were significantly higher in ileitis patients requiring surgery. In patients starting on biological therapy, the UPR scores did not change in clinical and endoscopic non-responders but did change in the patients with endoscopic response when inflammation resolved.
Conclusions: We developed a multi-facetted scoring system in CD patients to molecularly characterize disease by the degree of dysbiosis and dysregulation of the immune proteome as well as the intestinal barrier integrity. We further showed the dynamic of certain components of this score with regards to therapy response. Therefore, molecular characterization of patients could be a novel individualized approach to CD management. Additional validation in an independent cohort is essential.
References: 1. Gevers, D. et al. The treatment-naive microbiome in new-onset Crohn's disease. Cell Host Microbe 15, 382–392 (2014).

- I05 -

MATRIX GLA PROTEIN, A POTENTIAL MARKER OF TISSUE REMODELLING AND PHYSIOLOGICAL AGEING OF THE GUT IN CROHN'S DISEASE. S. Vieujean (1), P. Delanaye (2), L. Seidel (3), E. Cavalier (4), N. Pierre (5), E. Louis (1) / [1] CHU of Liège, Belgium, Hepato-Gastroenterology and Digestive Oncology, [2] CHU of Liège, Belgium, Dialysis-Nephrology-Transplantation, [3] CHU of Liège, Belgium, Biostatistics and medico-economic information, [4] CHU of Liège, Belgium, Clinical Chemistry, [5] University of Liège, Belgium, Laboratory of Translational Gastroenterology.

Introduction: Matrix Gla protein (MGP) is an extracellular matrix protein. The inactive dephosphorylated and uncarboxylated form of this protein, called dp-ucMGP, has been shown to be increased in plasma of Crohn's disease (CD) patients compared to non inflammatory bowel disease patients (Brnic et al., 2020).
Aim: Our aim was to assess if the plasmatic level of dp-ucMGP could reflect disease endoscopic activity and could be a potential marker of mucosal healing in CD.
Methods: The plasmatic level of dp-ucMGP was measured in a blood sample collected the same day as the ileocolonoscopy by CLIA method using IDS-iSYS InaKtif MGP. In addition to classical clinical data (gender, age, body mass index or BMI, disease duration, IBD treatment), endoscopic (disease localisation, Crohn's Disease endoscopic index or CDEIS, as well as the presence of erythema, ulcer, oedema, pseudopolyp, stricture) and biological (C-reactive protein or CRP) parameters were collected as well as faecal calprotectin to assess CD activity.
Results: A total of 82 colonoscopies and dp-ucMGP assays were performed in 75 CD patients (44 females and 31 males; 43 colonic diseases, 22 ileal diseases and 19 ileocolic diseases) between October 2012 and November 2019. Out of the 82 performed colonoscopies, 22 showed a mucosal healing. Although MGP level was significantly correlated with CDEIS (r=0.21, p=0.040), it was neither associated with endoscopic remission (737 ± 205 pmol/L for patients in endoscopic remission vs 809 ± 332 pmol/L for those who were not, p=0.37), nor correlated with faecal calprotectin (r=0.074, p=0.51) or with CRP (r=0.12, p=0.27) levels. Plasma MGP levels increased significantly with age (r=0.38, p=0.0004) and disease duration (r=0.37, p=0.0006) but not with the BMI (r=0.045, p=0.69). Patients on corticosteroids at the time of colonoscopy had a higher level of MGP (1065 ± 531 pmol/L vs 729 ± 179 pmol/L, p=0.0003). There was no association with other treatments (5-ASA, immunomodulators, anti-TNF, anti-α4β7 integrin or anti-IL-12/IL-23 p40 monoclonal antibody). Regarding endoscopic CD lesions, MGP values were significantly higher in cases of oedema (1153 ± 628 pmol/L vs 766 ± 261 pmol/L, p=0.019) and pseudopolyps (1099 ± 569 pmol/L vs 766 ± 264 pmol/L, p=0.018) but there was no association with the presence of other lesions.
Conclusions: The significant increase of plasmatic MGP levels with age, disease duration but also in patients with pseudopolyps suggests that this extracellular matrix protein could rather be a marker of tissue remodelling (not necessarily stricturing) and physiological ageing of the gut in CD than a marker of disease activity. The relevance of the plasmatic dosage of this protein to assess CD bowel damages deserves to be further investigated.

- I06 -

A RANDOMIZED PLACEBO CONTROLLED CLINICAL TRIAL WITH 5-HYDROXYTRYPTOPHAN IN PATIENTS WITH QUIESCENT INFLAMMATORY BOWEL DISEASE AND FATIGUE (TRP-IBD). M. Truyens (1), T. Lobaton Ortega (2), A. Peeters (2), M. Ferrante (3), S. Vermeire (3), P. Bossuyt (4), L. Pouillon (4), P. Dewint (5), A. Cremer (6), H. Peeters (7), G. Lambrecht (8), E. Louis (9), J. Rahier (10), O. Dewit (11), V. Muls (12), T. Holvoet (13), L. Vandermeulen (14), G. Gonzales (15), D. Laukens (1), M. De Vos (1) / [1] Ghent University, Ghent, Belgium, Internal Medicine and Pediatrics, [2] Ghent University Hospital, Ghent, Belgium, Gastroenterology and Hepatology, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [4] Imelda Hospital, Bonheiden, Belgium, Imelda GI Clinical Research Center, [5] Maria Middelares Ziekenhuis, Gent, Belgium, Gastroenterology, [6] Erasme Hospital, Brussels, Belgium, Gastroenterology, [7] AZ Sint-Lucas, Ghent, Belgium, St-Lucas IBD Clinic, [8] AZ Damiaan, Oostende, Belgium, Gastroenterology, [9] CHU Liège University Hospital, Liège, Belgium, Gastroenterology, [10] CHU UCL Namur, Yvoir, Belgium, Gastroenterology, [11] UCL Saint Luc, Brussels, Belgium, Service d'Hépato-Gastroentérologie, [12] Saint-Pierre University Hospital Center, Université Libre de Bruxelles (ULB), Brussels, Belgium, Gastroenterology and Endoscopy, [13] AZ Nikolaas, Sint-Niklaas, Belgium, Gastroenterology, [14] Universitair Ziekenhuis Brussel, Brussel, Belgium, Gastroenterology and Hepatology, [15] Wageningen University and Research, Wageningen, The Netherlands, Nutrition, Metabolism and Genomics Group, Division of Human Nutrition and Health.

Introduction: Fatigue is highly prevalent in patients with IBD independent of the disease status, but treatment options remain limited. A potential mediator in the pathophysiology of fatigue is tryptophan (Trp), a precursor of serotonin. Recently, reduced serum Trp levels have been linked to fatigue in patients with clinically and endoscopically inactive IBD.
Aim: The aim of the current study was to determine the effect of oral 5-hydroxytryptophan (5-HTP), the direct precursor of serotonin, supplementation on fatigue in patients with inactive IBD.
Methods: This multicentre, randomized, double-blind, cross-over, placebo-controlled trial included fatigued patients with IBD in clinical and biochemical remission (CRP <10mg/L, calprotectin <250 mg/kg), treated with immunosuppressants and/or biologicals. Fatigue was assessed with the fatigue VAS (fVAS, range 0-10) and defined by a fVAS ≥5. Patients were treated in a cross-over manner with 100 mg 5-HTP or placebo bid for two consecutive periods of 8 weeks, without an intermediate washout period. The primary endpoint was the proportion of patients reaching a 20% reduction in fVAS after 8 weeks of intervention (week 8 versus week 0 and week 16 versus week 8). Secondary outcomes were changes in validated FACIT-F score, scores for depression and anxiety and changes in Trp metabolites. The effect of the intervention on the outcomes was evaluated by linear mixed modelling (LMM), with the intervention, period and intervention x period as fixed factors and study participant as random factor.
Results: A total of 166 patients were included in 13 Belgian centres between December 2018 and November 2020; 82 patients were included in group A (5-HTP followed by placebo) and 84 patients in group B (placebo followed by 5-HTP). The median age was 39 years [IQR: 29.8 – 46], 94 patients (56.6%) were female and 120 (72.3%) of patients had Crohn's disease. Baseline characteristics were comparable between both study groups. In group A the baseline fVAS was 6.67 (SD 0.98), in group B 6.71 (SD 1.06) (p=0.784). The dropout rate was 10.8%. The evolution of the fVAS throughout the study was comparable between both study groups and the proportion of patients reaching ≥20% reduction in fVAS did not differ between placebo (37.6%) and 5-HTP (35.6%) (p=0.830). When using a LMM approach the fVAS reduction was comparable between 5-HTP and placebo treatment (estimate -0.19 [-1.00 – 0.62], p=0.645). The evolution of the FACIT-F (estimate 0.97 [-2.94 – 4.88], p=0.626) and the scores for depression (estimate -0.42 [-2.99 – 2.14], p=0.746), anxiety (estimate 1.35 [-0.59 – 3.29], p=0.170) and stress (estimate -0.14 [-2.85 – 2.58], p=0.921) were also similar between placebo and 5-HTP. A significant increase in 5-HTP (estimate 64.59 [47.36 – 81.82], p<0.001) and serotonin (estimate 3.41 [2.34 – 4.49], p<0.001) serum levels was observed during 5-HTP treatment compared to placebo; whereas serum levels of Trp (estimate 0.50 [-4.84 – 5.84], p=0.845) and kynurenine (estimate -0.04 [-0.37 – 0.30], p=0.827) were comparable. Globally, changes in fVAS were not associated with changes in those metabolites. Adverse events (AEs) were seen in 29.2% and 34.8% of patients under treatment with placebo and 5-HTP respectively (p=0.282).
Conclusions: Despite a significant increase in serum 5-HTP and serotonin levels by oral treatment with 5-HTP, 5-HTP did not modulate IBD-related fatigue. Furthermore, treatment with 5-HTP had no impact on depression, anxiety and stress scores.

- I07 -

DISTINCT MOLECULAR PROFILES BETWEEN IDIOPATHIC CRYPTOGLANDULAR AND CROHN-RELATED PERIANAL FISTULAS. B. Verstockt (1), S. Verstockt (2), G. Bislenghi (3), J. Sabino (1), M. Ferrante (1), A. D'hoore (3), S. Vermeire (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Chronic Diseases and Metabolism, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Abdominal Surgery.

Introduction: Perianal fistula can originate idiopathically (cryptoglandular fistula) or can be a representation of underlying Crohn's disease (CD). In case of idiopathic fistula, the cryptoglandular theory suggests their development from the anal glands. In contrast, the pathophysiology of CD-related fistula is very poorly understood.
Aim: To molecularly characterise and compare the fistula tract in patients with Crohn's disease versus cryptoglandular, idiopathic fistula.
Methods: We collected surgical biopsies from the fistula tract in 70 CD patients with active draining perianal fistula and in 12 patients with cryptoglandular non-CD related, active draining fistula, all requiring surgical examination under anaesthesia. RNA was sequenced using Illumina HiSeq4000, and these data were analysed through differential gene expression analysis (DESeq2). A false discovery rate (FDR) of 0.05 and a |log 2-fold change (log2FC)| >1 was considered significant. Pathway analysis was performed using IPA (Qiagen). In addition, cellular deconvolution methods (xCell) were applied to study the cellular composition.
Results: Gene expression analysis identified 1087 genes being differentially expressed between CD-related and cryptoglandular fistula (716 up, 371 down). Top differentially expressed genes encode proteins implicated in IBD pathogenesis including CARD18 (log2FC= 23.2, p=3.9E-21), BATF2 (log2FC=2.8, p=1.8E-8), ETV7 (log2FC=2.1, p=2.0E-7), DSG1 (log2FC=7.8, p=2.7E-6) and IL22RA1 (log2FC=5.3, p=4.6E-6). Additional pathway analysis highlighted various proinflammatory processes in CD fistula (as compared to cryptoglandular fistula), including upregulation of antigen presentation and Th1/Th2 activation (p<1.0E-9). Intriguingly, CD fistula showed a significant downregulation of wound healing signaling pathways (p=6.5E-6), emphasising the refractory character of this debilitating condition. Upstream analyses showed an increased activation of top regulators IFNγ, TNF, LPS and STAT1 (p<1.0E-24). Cellular deconvolution identified significant differences between both fistula types, with a predominance of inflammatory cells in CD including Th1 cells, dendritic cells, naïve CD4 T cells, memory B cells and central memory CD8 and CD4 T cells (p<5.0E-2). In contrast, cryptoglandular fistula were characterised by a significant enrichment of myocytes, smooth muscle cells and neurons (p<3.0E-3). Presence of neutrophils, wound healing and pro-inflammatory macrophages did not differ between both fistula types.
Conclusions: CD fistulas have a strong proinflammatory fingerprint, but seem to have lower wound healing capacity as compared to cryptoglandular fistula. An aggressive medical and surgical treatment is therefore required, including the search for novel, powerful anti-inflammatory compounds.

- I08 -

EFFICACY AND SAFETY OF BONE MARROW-DERIVED MESENCHYMAL STEM CELLS IN REFRACTORY PERIANAL FISTULAE IN CROHN'S DISEASE: RESULTS FROM A PROSPECTIVE MONOCENTRIC STUDY.

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Introduction: Anoperianal lesions affect up to 30% of patients with Crohn's disease (CD). Long-term fistula healing is challenging with conventional biotherapies. Although recent studies demonstrated the efficacy of local injections of adipose tissue-derived stem cells with 50 % of fistulae closure without abscess at one year, this treatment is not available in routine.
Aim: The primary aim of this study was to evaluate the safety and the feasibility of the injection of bone marrow-derived mesenchymal stem cells isolated and prepared in a local university laboratory of cell therapy for perianal fistulizing CD. The second aim was to evaluate the efficacy of this treatment and his impact on the quality of life of the patients.
Methods: A prospective observational study was performed in the CHU of Liège from October 2019 till October 2021. All CD patients with perianal fistula and seton placement for at least 6 months were eligible. PRO, clinical examination, CRP, fecal calprotectine, CDAI, Short Health Scale (SHS) and pelvic MRI were performed at weeks 0, 12 and 48. PDAI was calculated at inclusion and at week 48. Efficacy was defined as closure of all treated external openings at clinical examination without abscess at MRI.
Results: Sixteen patients with a median age of 49 years and a median duration of perianal CD of 8 years were included. Eleven (69%) patients were on anti-TNF. Median CDAI and PDAI at inclusion were 97.5 +/- 48.8 and 5 +/-4.4 respectively. Four (25%) patients reported adverse events the week after the injection (local pain 3/16, mild bleeding 1/16). Ten (63%) and 8 (50%) patients had a closure of all the external openings at week 12 and 48 respectively. Five out of 6 patients with 2 external openings had at least 1 opening closed at week 48. One abscess was observed during the follow-up. The median PDAI was numerically lower at the end of the study (3 versus 5 at the inclusion). The quality of life improved with a regression of the SHS from 10 to 7.5 at the end of the follow-up. MRI MAGNIFI-CD score and Van Assche index were similar at the inclusion and at the end of the study for each patients.
Conclusions: Injection of locally prepared bone marrow-derived mesenchymal stem cells seems safe and effective in refractory perianal fistulae in Crohn's disease with 50% of closure at 1 year. The treatment is associated with an improvement of the perianal activity index and the quality of life scores but not with the MRI scores.

- I09 -

CHANGES IN COLECTOMY FOR ULCERATIVE COLITIS DURING THE LAST TWO DECADES: AN IN-DEPTH RETROSPECTIVE ANALYSIS.

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Introduction: The management of ulcerative colitis (UC) has been improved due to progresses in medical and surgical practices during the past twenty years. Yet the impact of new therapies on the evolution of the three colectomy's indications in UC (severe acute colitis, refractory ulcerative colitis and (pre-)neoplastic complication) is still not well established.
Aim: The aim of this study was to describe and compare the evolution of the indications, procedures and complications of surgery among patients with UC who underwent a colectomy within the last two decades.
Methods: This was an observational retrospective study carried out in two tertiary hospitals. All patients with UC who underwent total or segmental colectomy between 2001 and 2020 were included, without age restriction. Two periods were compared: 2001-2010 and 2011-2020. Endpoints were to compare the colectomy indications, patients' characteristics, surgical procedures, and rates of postoperative complication between the two cohorts.
Results: Among the 286 patients included (57% were men; median age of 40 years; 60.5% of extensive and 35.7% of distal colitis), 87 (30.4%) underwent colectomy in 2001-2010 and 199 patients (69.6%) in 2011-2020. Patients' characteristics were similar between the two periods, including duration of UC and the severity according to the global Mayo score. Colectomy rate for refractory UC significantly decreased over time (n=119) (50.6% vs. 37.7%; p=0.042), while it increased for acute severe colitis (n=116) (36.8% vs. 42.2%; p=0.390) and (pre-)neoplastic indication (n=51) (12.6% vs. 20.1%; p=0.130). Regarding surgery, there was an increased use of laparoscopic colectomy (47.7% vs. 81.4%; p<0.001) during the latter period, and the median length of stay in hospital after surgery has decreased from 13 to 10 days (p=0,098). There were less early (12.6% vs. 5.5%; p=0.038) and late severe complications (1.6% vs. 0.8%; p< 0.001) and less surgical revisions (38.6% vs. 19.5%; p<0.001) without change on 30-day mortality rate (2.3% vs. 1%; p=0.391). The rate of extraintestinal postoperative infections (especially urinary, pulmonary and catheters infections) increased during the second period (27% vs; 45.7%; p=0.018). As expected, the mean number of past biotherapies was higher during the second period (1.2 versus 0.6; p<0.001), as well as the rate of pre-operative exposition to TNFα antagonists (68.4% vs. 50.6%; p=0.016).
Conclusions: The rate of surgery for refractory colitis has significantly decreased while the rate of colectomy for cancer and acute severe colitis has raised during the last twenty years. In the same time, surgical technics have changed with more laparoscopic surgeries associated with a reduction of postoperative morbidity despite the larger use of biotherapies.

- I10 -

EFFICACY AND SAFETY OF USTEKINUMAB FOR CHRONIC ANTIBIOTIC REFRACTORY POUCHITIS: A BELGIAN OPEN-LABEL MULTICENTRE PILOT STUDY.

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Introduction: Up to 10% of ulcerative colitis patients who undergo a proctocolectomy with ileal pouch-anal anastomosis, will develop chronic antibiotic refractory pouchitis (CARP).
Aim: As there is a large unmet need in the management of these patients, we evaluated the efficacy and safety of induction therapy with ustekinumab (UST) for this indication.
Methods: We performed a prospective, Belgian, multicentre, open-label study of patients with CARP. Patients received a weight-range-based infusion of UST at baseline (6mg/kg) and one subcutaneous injection of 90mg UST at week 8. The first 4 weeks, ciprofloxacin 500mg BID was added as bridging therapy, but need of antibiotics thereafter was regarded as treatment failure. Patients underwent pouchoscopy at baseline and week 16, with assessment of the modified pouchitis disease activity index (mPDAI). The primary endpoint was the proportion of patients achieving clinically relevant steroid-free remission (mPDAI <5 and reduction by ≥2 points from baseline) at week 16. Secondary endpoints at week 16 were the proportion of patients achieving response (reduction of mPDAI by ≥2 points from baseline), change in symptomatic and endoscopic mPDAI subscore, and change in C-reactive protein (CRP) and faecal calprotectin levels compared to baseline. Descriptive statistics and paired nonparametric tests (Wilcoxon signed-rank) of changes from baseline were performed.

Results: We report the first 18 patients (56% male, median age 41.5 years, median time after surgery 11.2 years) who reached the primary endpoint assessment. Eleven (61.1%) patients had previously been treated with biologics (anti-TNF, n=8; vedolizumab, n=6; tofacitinib, n=1) for CARP. At week 16, clinically relevant steroid-free remission was reached in 27.8% and response in 50.0% of patients. A significant decrease in total mPDAI (8.0 (7.0-8.3) vs. 6.5 (3.8-9.0), p=0.04) and clinical subscore (3.0 (2.0-4.0) vs. 2.0 (1.0-3.3), p=0.04) but not endoscopic subscore (5.0 (4.0-6.0) vs. 4.0 (3.0-6.0), p=0.1) was observed at week 16. Faecal calprotectin (288.0 (154.8-634.8) vs. 145 (88.3-749.3) mg/kg, p=0.47) and CRP (4.8 (1.9-7.2) vs. 3.9 (1.9-8.9) mg/L, p=0.63) levels did however not decrease significantly. Three serious adverse events (hospitalization for subobstruction, worsening pouchitis and choledocholithiasis) were recorded, but were not considered related to UST.
Conclusions: In this open-label pilot study in patients with CARP, induction therapy with UST showed a clinical effect in half of the patients, but was not associated with endoscopic improvement or changes in inflammatory biomarkers. Placebo-controlled studies are needed for further positioning UST in the treatment algorithm of CARP.

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REAL-WORLD EFFECTIVENESS AND SAFETY OF RISANKIZUMAB IN PATIENTS WITH MODERATE-TO-SEVERE MULTI-REFRACTORY CROHN'S DISEASE: A BELGIAN MULTI-CENTRIC COHORT STUDY. D. Alsoud (1), D. Franchimont (2), F. D'heygere (3), P. Bossuyt (4), A. Vijverman (5), P. Van Hootegem (6), J. Sabino (7), A. Cremer (8), S. Vermeire (7), M. Ferrante (7) / [1] KUL - University of Leuven, Leuven, Belgium, Translational Research in Gastrointestinal Disorders, Department of Chronic Disease, Metabolism and Ageing, [2] Erasme Hospital, Brussels, Belgium, Department of Gastroenterology, [3] AZ Groeninge, Kortrijk, Belgium, Department of Gastroenterology, [4] Imelda Hospital, Bonheiden, Belgium, Department of Gastroenterology, [5] CHR Citadelle, Liège, Belgium, Department of Gastroenterology, [6] AZ Sint-Lucas Brugge, Assebroek/ Brugge, Belgium, Department of Gastroenterology, [7] University Hospitals Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology, [8] Erasme Hospital, Brussels, Belgium, Department of Gastroenterology.

Introduction: In recent phase 3 trials, risankizumab (RZB), a humanised monoclonal IgG1 antibody targeting the interleukin 23 p19 subunit, proved to be superior to placebo in inducing and maintaining clinical remission and endoscopic response in patients with moderate-to-severe Crohn's disease.
Aim: To evaluate the effectiveness and safety of RZB in a real-world cohort of multi-refractory CD patients.
Methods: Adult CD patients from six Belgian IBD centres who initiated RZB prior to May 2021 as part of a medical need program were prospectively followed. Patients with an ostomy were excluded for the main analyses. The primary endpoint was steroid-free clinical remission at week 24 (average daily liquid stool frequency [SF] ≤2.8 and average abdominal pain [AP] score ≤1, both not worse than baseline). Secondary endpoints included clinical response (≥ 30% decrease in average daily SF and/or ≥ 30% decrease in average daily AP score, both not worse than baseline), endoscopic remission (simple endoscopic score for Crohn's disease [SES-CD] ≤ 4), endoscopic response (≥ 50% decrease in SES-CD), biological remission (CRP ≤ 5 mg/L, only for patients with a baseline CRP > 5 mg/L), biological response (≥ 50% decrease in CRP, only for patients with a baseline CRP > 5 mg/L), need for CD-related hospitalisation or surgery, and serious adverse events. Given that a follow-up endoscopy has not yet been performed in some patients, results are shown for both "all patients" (with non-responder imputation) and "as observed".
Results: A total of 27 patients started RZB of whom 19 patients were eligible for this study with a minimal follow-up of 24 weeks. Eight patients were excluded as they had an ostomy at time of RZB initiation. Eighteen patients (95%) had been exposed to more than 3 biologicals and 13 (68%) previously underwent a CD-related intestinal resection. By week 24, 7/19 (37%), 7/19 (37%), 15/19 (79%), 1/19 (5%), 3/19 (16%), 10/19 (53%) patients achieved steroid-free clinical remission, endoscopic response, clinical response, endoscopic remission, biological remission and biological response, respectively. In the "as observed" analyses, these rates were 7/18 (39%), 7/9 (78%), 15/18 (83%), 1/9 (11%), 3/16 (19%), 10/16 (63%), respectively. Five patients used concomitant steroids at baseline and were all able to stop it after a median of 10 weeks. Eventually, three patients had to be hospitalized for bowel resection (2 with placement of an ostomy) after a median of 24 weeks, two of them required earlier an emergent hospitalization due to flares of abdominal pain and bloody diarrhea. None of the patients experienced serious infections or intolerance. Based on physician global assessment, three out of eight patients with an ostomy did achieve clinical remission, and two other achieved clinical response. Endoscopic follow-up data were available in six patients, and three of them experienced endoscopic response.
Conclusions: In this real-world, multi-refractory cohort, clinical remission and endoscopic response were both observed by week 24 in more than one third of CD patients initiating RZB. RZB was well tolerated with no safety issues.

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REAL-WORLD ENDOSCOPIC AND HISTOLOGIC OUTCOMES ARE LINKED TO USTEKINUMAB EXPOSURE IN ULCERATIVE COLITIS. D. Alsoud (1), G. Compernolle (2), S. Tops (2), J. Sabino (3), M. Ferrante (3), D. Thomas (2), G. De Hertogh (4), S. Vermeire (3), B. Verstockt (3) / [1] KUL - University of Leuven, Leuven, Belgium, Translational Research in Gastrointestinal Disorders, Department of Chronic Disease, Metabolism and Ageing, [2] KUL - University of Leuven, Leuven, Belgium, Laboratory for Therapeutic and Diagnostic Antibodies, Department of Pharmaceutical and Pharmacological Sciences, [3] University Hospitals Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology, [4] University Hospitals Leuven, Leuven, Belgium, Laboratory of Morphology and Molecular Pathology.

Introduction: Histologic healing is being proposed as new treatment target in ulcerative colitis (UC), and the concept of histo-endoscopic mucosal improvement was introduced in the UNIFI study with ustekinumab (UST) in moderate–to-severe UC. Very little is known about the Pk-PD relationship of ustekinumab in UC patients, and especially whether serum UST concentrations correlate well with colonic tissue drug exposure and with histologic healing.
Aim: To provide real-world data including histology, and to study UST serum concentrations and its relation to tissue levels and drug efficacy.
Methods: UC patients starting UST in standard dosage at our referral centre were prospectively followed by clinical and endoscopic assessments at week 16 or week 24, and colonic biopsies were taken for histopathologic scoring. Histologic remission was defined as Nancy histology index (NHI) of 0. Other collected outcomes were clinical response (decrease in partial Mayo score [PMS] of ≥2 points, plus a decrease in rectal bleeding subscore of ≥1 point or an absolute rectal bleeding subscore of 0 or 1), clinical remission (PMS of ≤2 with no individual subscore >1, and a rectal bleeding subscore of 0), endoscopic improvement (Mayo endoscopic sub-score [MES] of ≤1), endoscopic remission (MES of 0) and mucosal healing (combination of endoscopic and histologic remission). Paired trough serum sample and colonic mucosal biopsy were collected for UST levels measurement using a CE marked in-house developed ELISA.
Results: A total of 42 UC patients started ustekinumab between June 2019 and May 2021, allowing a follow-up of at least 6 months. By week 24, clinical response, clinical remission, endoscopic improvement, endoscopic remission, and mucosal healing were observed in 31 (74%), 24 (57%), 22 (52%), 11 (26%) and 10 (24%) patients, respectively. Histologic remission was observed in 19 (45%) patients, of whom 10 and 9 with endoscopic Mayo 0 and 1, respectively. Multivariate analysis identified clinical response at week 8 as a predictor for histologic remission at week 24 [OR 8.84, p = 0.024], and inversely correlated with therapy discontinuation [OR 0.10, p = 0.006]. A trend of higher UST serum trough levels was observed in patients achieving histologic and endoscopic outcomes in comparison with patients who did not reach these outcomes, with a significant statistical difference at week 8 for endoscopic outcomes (p = 0.009 for endoscopic improvement, P = 0.0067 for endoscopic remission). UST concentrations from paired serum and biopsy samples revealed a strong positive correlation (Spearman r=0.88, p<0.001, n=17), both in inflamed (mayo endoscopic score >1) (r=0.89, p<0.001, n=10) and uninflamed (mayo endoscopic score ≤ 1) tissue (r=0.88, p<0.008, n=7).
Conclusions: In this real-word cohort of UC patients initiating UST, more than a third of the patients achieved histologic remission. Serum UST levels were furthermore strongly correlated with tissue levels of UST. A drug exposure-response relationship was observed for histologic and endoscopic outcomes.

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POSITIONING OF USTEKINUMAB AFFECTS ITS EFFECTIVENESS, DRUG PERSISTENCE AND SERUM EXPOSURE IN CROHN'S DISEASE. D. Alsoud (1), J. Sabino (2), M. Ferrante (2), S. Vermeire (2), B. Verstockt (2) / [1] KUL - University of Leuven, Leuven, Belgium, Translational Research in Gastrointestinal Disorders, Department of Chronic Disease, Metabolism and Ageing, [2] Univeristy Hospitals Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Ustekinumab (UST), an anti-IL12/23p40 monoclonal antibody, has been approved for treating Crohn's disease (CD). As for all biologicals, efficacy is reduced in patients with previous anti-TNF exposure.
Aim: To investigate whether UST outcomes and serum exposure are affected by UST positioning as first-, second-, or third-line biological treatment and type of previous biologicals (anti-TNF biologicals and vedolizumab [VDZ]).
Methods: Data on primary (non)-response, drug persistence and serum trough levels were collected from CD patients who started UST as a first-, second-, or third-line biological treatment from December 2015 through October 2020, allowing a follow-up of ≥12 months. Differences in rates of primary non-response (< 50% decrease in SES-CD and absence of any clinical improvement) after 6-12 months, and UST persistence were compared based on UST positioning and previous biologicals. Finally, we compared serum UST exposure profiles between groups.
Results: A total of 181 CD patients with active disease started UST as first- (n=41; 22.65%), second- (n=57, 31.5%) or third-line (n=83, 45.85%), respectively. Of second-line UST starters, 52 (28.7%) patients were exposed to one anti-TNF biological and 5 (2.8%) to vedolizumab. Of third-line UST starters, 41 (22.65%) patients were exposed to both one anti-TNF and VDZ, while 42 (23.2%) were exposed to two anti-TNFs. Second-line UST starters with previous VDZ were excluded from further analysis due to small sample size (n=5). A gradual decrease in response rates (p=0.02) and drug persistence (p=0.03) was observed with increasing lines of biologicals given prior to start UST, with patients starting UST as third-line treatment after two anti-TNFs having the highest rates of primary non-response (43%) and the shortest drug persistence. This finding was paralleled by a progressive decrease in UST serum levels with increasing number of previous biologicals and number of previous anti-TNFs, in 71 patients of whom induction and maintenance UST serum levels were available.

Conclusions: Both short term response rates, as well as long term UST persistence rates, decreased with increasing lines of previous biological therapies. Patients exposed to two anti-TNFs had worse UST outcomes on short-term and long-term, and lower serum trough levels than patients who received only one or no anti-TNF biological before or prior VDZ exposure. These data help in positioning UST in CD and in framing the discussion with patients.

- I14 -

PREVALENCE AND OUTCOMES OF SARS-COV2 INFECTION IN PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY DISEASES (IMID): A MONOCENTRIC BELGIAN POPULATION-BASED RETROSPECTIVE STUDY. C. Vuckovic (1), A. Hoyois (2), J. Mungwete (2), L. De Bellefon (3), C. Musala (2), J. Massart (2), S. Di Romana (3), V. Muls (2) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology, [2] Saint-Pierre University Hospital Center, Université Libre de Bruxelles (ULB), Brussels, Belgium, Gastroenterology, [3] Saint-Pierre University Hospital Center, Université Libre de Bruxelles (ULB), Brussels, Belgium, Rheumatology.

Introduction: Prevalence and severity of Sars-Cov2 infection in IMID population does not seem to differ from the general population. Data suggest that older age and comorbidities are associated with a poor outcome, as seen in the general population. Corticosteroids, combo-therapies (especially tumor necrosis factor (TNF) antagonists and thiopurines) are associated with an increased risk of severe Sars-Cov2 while TNF antagonists alone do not impact the risk, as reported by the Surveillance Epidemiology of Coronavirus Under Research Exclusion for Inflammatory Bowel Disease (IBD) database. However, no study has been conducted in Belgium where the Sars-Cov2 morbidity and mortality rate has been ranked among the highest in the world during the first wave.
Aim: The aim of this monocentric retrospective study is to assess the prevalence of Sars-Cov2 infection in the IMID population, to evaluate the severity of Sars-Cov2 infection and the potential role of IMID medication classes as risk factor for severe infection.
Methods: Patients treated in Saint-Pierre University Hospital, Brussels, were invited to fill in a questionnaire during an outpatient clinic appointment from March 2020 till May 2021, to assess their current treatment regimens and whether they have had symptoms compatible with Sars-Cov2 infection. Confirmed infection was defined by positive PCR test or positive serologic test. Data were collected and analyzed retrospectively. Key variables included demographics, smoking status, comorbidities, IMID details and Sars-Cov2 status. Comparison of Sars-Cov2 infection prevalence in the IMID population was performed with the general Belgian population using Sciensano database. Demographic, clinical characteristics and COVID-19 outcomes of the study population were summarized by using descriptive statistics. Continuous variables were reported by using median and interquartile range (IQR), and categorical/dichotomous variables were reported as number and percentage. Differences between the groups of patients were investigated by Fisher's exact test and Chi-squared test, as appropriate.
Results: 265 IMID patients were included. Median age was 50 years (IQR= 20). There was a predominance of females (n = 161 [61%]). The most commonly reported comorbidities were obesity (n = 59 [22%]), hypertension (n = 58 [22%]), diabetes (n = 19 [7%]), pulmonary disease (n = 22 [7%]) and cancer (n = 13 [5%]). A total of 62 patients smoked (23%). Main IMID reported were Rheumatoid Arthritis (n = 68 [25%]), Crohn's Disease (n = 67 [25%]), Psoriatic Arthritis (n = 49 [18%]), Ankylosing Spondylitis (n = 48 [18%]) and Ulcerative Colitis (n = 35 [13%]). 19 patients had multiple IMID (7%). Most patients were receiving a biologic treatment (n= 151 [57%]). Of those, 20% were on combotherapy with Azathioprine or Methotrexate. 35 patients were on Methotrexate therapy alone (13%) and 10 patients were on Azathioprine monotherapy (4%). 53 patients (20%) were treated by corticotherapy. Of the 265 patients, 24% had symptoms compatible with Sars-Cov2 infection and 62% of those were confirmed with Sars-Cov2 infection, which represents 14% of the total IMID population. There was 10% of SARS-Cov2 infection in the Belgian population in the same time frame and there was no statistical difference between those 2 populations ($p < 0,05$). In the subgroup of IBD patients (n=101), 18% had confirmed Sars-Cov2 infection. We observed no severe Sars-Cov2 infection nor death within our population. Only two patients were hospitalized for an extrapulmonary manifestation of the Sars-Cov2 infection. There was no statistical difference between infected and non-infected groups for comorbidities. Type of treatment for IMID patients was not associated with a significantly increased risk for Sars-Cov2 infection. After subgroup analysis, the IBD subgroup (n=101) showed a significantly higher prevalence of Sars-Cov2 infection when treated by anti-Integrin or anti-Interleukine therapy (55% vs 29%, p-value < 0,05). Median age and comorbidities in IBD patients treated by anti-Interleukine or anti-Integrin therapy did not statistically differ from the IBD population on other treatment regimens.
Conclusions: Prevalence of Sars-Cov2 infection in our cohort of IMID patients was similar to the Belgian population, despite relatively high percentage of patients under biologic therapy. Type of treatment for IMID patients was not associated with a significantly increased risk of SARS-Cov2 infection, although a significantly higher prevalence of SARS-Cov2 infection was found in the IBD subgroup treated by anti-Interleukine or anti-Integrin.

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EVALUATING SEGMENTAL HEALING WITH THE MODIFIED MAYO ENDOSCOPIC SCORE (MMES) HAS A CLEAR ADDITIONAL VALUE IN PREDICTING LONG-TERM OUTCOME IN PATIENTS WITH ULCERATIVE COLITIS: RESULTS FROM A PROSPECTIVE COHORT STUDY. M. Lenfant (1), B. Verstockt (2), J. Sabino (2), S. Vermeire (2), M. Ferrante (2) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Chronic Diseases, Metabolism and Ageing, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology.

Introduction: Endoscopy has a pivotal role in evaluating disease activity in ulcerative colitis (UC). However, most endoscopic scoring systems (including the Mayo endoscopic subscore, MES) do not consider the extent of UC involvement and can therefore not pick up segmental endoscopic improvement. The modified Mayo endoscopic score (MMES) was developed to overcome this limitation. The MMES is calculated by multiplying the Mayo endoscopic subscore for the different colon segments (ascending, transverse, descending, sigmoid and rectum) with the maximal extent of inflammation (in decimeters) divided by the number of segments with active inflammation (Lobatón T, et al. J Crohn's- Colitis 2015; 9:846–52).
Aim: We examined the predictive value of the MMES in addition to the MES on long-term clinical outcomes in UC.
Methods: Between January 2014 and September 2017, patients initiating biologic therapy for active UC (baseline MES ≥ 2) were recruited at our tertiary referral center. Patients without assessment of the upper margin of inflammation or with a clinical follow-up <12 months were excluded. We conducted a clinical and endoscopic assessment at baseline and week 8 (adalimumab, ADM) or 14 (golimumab, GOL; infliximab, IFX; vedolizumab, VDZ). Clinical response was defined as a decrease in the adapted Mayo score (excluding physician global assessment) with ≥2 points and ≥30%, plus a decrease in rectal bleeding score ≥1 or an absolute rectal bleeding score ≤1. We classified patients by evolution of endoscopic activity at week 8/14 in group A (endoscopic healing, MES ≤1), group B (segmental healing, MES >1 but decrease in MMES ≥30%) and group C (MES >1 and no drop in MMES ≥30%). Clinical relapse-free, discontinuation-free and colectomy-free survival were estimated by Kaplan-Meier analysis with log-rank test. Clinical relapse was defined as need for any treatment optimization.
Results: A total of 150 consecutive UC patients were included (52% male, median age 42 years, median disease duration 7 years) with a median (IQR) follow-up of 61 (48-68) months. An anti-TNF was initiated in 74 (35 IFX, 23 ADM, 16 GOL), and VDZ in 76 patients. A significant reduction in MES [3 (IQR 2-3) to 2 (1-3), $p < 0.001$] and MMES [8.54 (5.19-13.33) to 5.13 (1.00-10.00), $p < 0.001$] was observed at week 8/14. In group A 67/69 (97%) patients achieved clinical response compared to 15/27 (55%) in group B and 11/54 (20%) in group C. During follow-up 60/93 (65%) patients maintained clinical response, 83/150 (55%) patients discontinued treatment due to primary non-response or loss of response and 33/150 (22%) patients underwent colectomy. The ΔMMES demonstrated to be of additional predictive value in long-term UC outcome: there was a significant difference in the Kaplan-Meier curve between groups B and C regarding clinical relapse ($p = 0.037$), drug persistence ($p < 0.001$) and need for colectomy ($p < 0.001$). Patients in group A had the best long-term outcome, but a clear trend for reduced treatment discontinuation and especially for reduced clinical relapse and colectomy rates was observed in group B.
Conclusions: Although endoscopic improvement (MES ≤1) remains the best predictor of long-term outcome, the MMES - identifying a subgroup with segmental endoscopic response - demonstrated a clear additional value predicting long-term outcome in UC. These promising results merit inclusion of the MMES in future clinical trials.

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PROPHYLACTIC VERSUS ENDOSCOPY-DRIVEN TREATMENT OF CROHN'S POSTOPERATIVE RECURRENCE: A RETROSPECTIVE, MULTICENTRIC EUROPEAN STUDY. J. Geldof (1), M. Truyens (1), M. Hanssens (1), T. Holvoet (2), A. Elorza (3), V. Bouillon (4), V. Martins (5), K. Argyriou (6), M. Diculescu (7), A. Moens (8), E. Theodoraki (9), J. Pedro (10), P. Nikolaou (11), F. Baert (12), R. Ferreiro-Iglesias (13), H. Peeters (14), M. Casanova (15), P. Eder (16), R. Porter (17), T. Karakan (18), F. Mesonero (19), J. Revés (20), E. Van Dyck (21), A. Jauregui-Amezaga (22), M. Mañosa (23), P. Rivière (24), L. Mosquera (25), F. Portela (26), T. Lobaton (1) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Department of Gastroenterology and Hepatology, [2] AZ Nikolaas, Sint-Niklaas, Belgium, Department of Gastroenterology , [3] Hospital Universitario de Galdalko, Galdalko, Spain, Department of Gastroenterology, [4] Erasme Hospital, Brussels, Belgium, Department of Gastroenterology, [5] Algarve Universitary Hospital Center, Faro, Portugal, Department of Gastroenterology, [6] University Hospital of Larisa, Larisa, Greece, IBD unit, Department of Gastroenterology, Faculty of Medicine, School of Health Sciences, University of Thessaly, [7] Carol Davila University of Medicine Bucharest., Bucharest, Romania, Gastroenterology and Hepatology Center Fundeni Clinical Institute, [8] Imelda Hospital, Bonheiden, Belgium, Department of Gastroenterology, [9] University Hospital Heraklion, Heraklion, Greece, Department of Gastroenterology, [10] Hospital Santa Maria, Centro Hospital Universitario de Liboa Norte, Lisbon, Portugal, Department of Gastroenterology and Hepatology, [11] Venizeleio General Hospital, Heraklion, Greece, Department of Gastroenterology, [12] AZ Delta, Roeselare, Belgium, Department of Gastroenterology and Hepatology, [13] Hospital Clinico Universitario de Santiago, Fundacion Instituto de Investigacion, Santiago de Compostela, Spain, Inflammatory Bowel Disease Unit, Department of Gastroenterology, [14] AZ Sint-Lucas, Ghent, Belgium, Department of Gastroenterology, [15] Hospital Universitario de La Princesa, Instituto de Investigacion Sanitaria Princesa IIS-IP and Centro de Investigacion Biomedica en Red de Enfermedades Heptaticas y Digestivas CIBERehd, Madrid, Spain, Gastroenterology unit, [16] Poznan University of

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Introduction: The risk of endoscopic postoperative recurrence (ePOR) remains high within 1 year after ileocaecal resection (ICR) for ileal Crohn's disease (CD). Currently, there is no consensus in how to reduce risk of ePOR, clinical(c)POR or surgical(s)POR on long-term.
Aim: This study aims to evaluate the impact of two strategies on POR: early medical prophylaxis (proactive strategy) versus treatment driven by findings at elective endoscopy 6-12 months after ICR (reactive strategy).
Methods: A retrospective, observational, multicentre, superiority study was performed including CD patients undergoing first ICR between 2008 and 2019. Patients were assigned to cohort 1 if prophylactic medical therapy was administered early after ICR, or to cohort 2 if no postoperative prophylaxis was started and medical treatment was driven by endoscopic findings 6-12 months after ICR. The primary endpoint was the rate of ePOR evaluated at ileocolonoscopy 6-12 months post ICR and was defined as Rutgeerts score >i1. Statistical analyses were performed with SPSS version 27.
Results: In total 336 patients were included from 26 centres in 9 European countries. Cohort 1 contained 48.8% and cohort 2 51.2% of all patients. Median age was 34 years old (range 26.0-44.0 years old) and median preoperative disease duration was 3 years (range 0-9.0 years). Of all patients, 30.4% had penetrating disease phenotype (Montreal B3) and 34.2% were actively smoking at time of surgery. Preoperatively, 33% of all patients were treated with an immunosuppressant, 35.2% were on anti-TNF, 3% on ustekinumab, 3% on vedolizumab and 32.7% was using corticosteroids. Cohort 1 and cohort 2 were comparable considering gender, age, smoking status, disease duration, disease phenotype, indication for surgery and biochemical markers of inflammation. Preoperatively, immunosuppressants and anti-TNF were more frequently used in cohort 1. There was no significant difference in postoperative complications between the two cohorts. Most frequently observed complications were intra-abdominal abscess (3.9%), bleeding (3.6%), wound infection (3.3%) and anastomotic leak (3.3%). Univariate logistic regression analysis showed a significantly higher rate of ePOR at endoscopy 6-12 months after surgery in cohort 2 patients (OR 2.03, 95%CI 1.30-3.18; P=0.002). Multiple logistic regression analysis with adjustment for age, smoking status, preoperative medical treatment, disease activity, surgical indication and propensity score (including differences per country) confirms the significant difference between cohort 1 and 2 (OR 1.87, 95%CI 1.10-3.16; P=0.02). Sub-analysis of the subgroup of patients with non-penetrating phenotype (Montreal B1 or B2) again confirmed this observation (OR 2.26, 95%CI 1.05-4.86; P=0.038).
Conclusions: In this retrospective, European multicentre study, initiation of medical treatment in patients with Crohn's disease immediately after ileocaecal resection was associated with a lower risk of endoscopic postoperative recurrence 6-12 months after surgery compared to endoscopy-driven treatment.

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VACCINATION COVERAGE SIGNIFICANTLY INCREASED AFTER IMPLEMENTATION OF A VACCINATION TOOL IN THE ELECTRONIC PATIENT HEALTH RECORD. L. Fierens (1), E. De Dycker (2), J. Joly (3), T. Vanhoutvin (4), P. Verschueren (3), P. De Haes (4), P. De Munter (5), J. Sabino (2), S. Vermeire (2), M. Ferrante (2) / [1] KUL - University of Leuven, Leuven, Belgium, Translational Research Center for Gastrointestinal Disorders (TARGID), Department of Chronic Diseases, Metabolism, and Ageing, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Rheumatology, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Dermatology, [5] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of General Internal Medicine.

Introduction: Patients with immune-mediated inflammatory diseases (IMID) are at higher risk for infectious diseases. Despite this increased risk and the available guidelines1, we reported a suboptimal vaccination rate of 33.8% of IMID patients in 2018. In the meantime, a vaccination module was introduced in the electronic patient health record of our hospital to accurately document and monitor vaccination status of patients.
Aim: To evaluate the impact of this new module, the vaccination coverage was re-evaluated in the same IMID patients in 2021.
Methods: Between Aug and Oct 2021, the vaccination status of 1448 (out of the original 1488) IMID patients (44.8% male, median age 53.6 years) was collected (798 patients with IBD, 612 with rheumatological, and 38 with dermatological inflammatory conditions) and compared to that of 2018. The vaccination status was obtained mainly through the patients' electronic medical records. Missing data were added after contacting patients or their general practitioner.
Results: From 2018 to 2021, the vaccination coverage of all IMID patients significantly increased from 73.1% to 81.9% for influenza, from 56.4% to 86.7% for pneumococci, from 52.3% to 63.6% for hepatitis B, from 71.4% to 85.9% for tetanus and from 33.8% to 51.1% overall (all p<0.001). The vaccination coverage in IBD patients increased significantly from 75.9% to 86.3% for influenza, from 72.9% to 88.7% for pneumococci, from 66.0% to 80.2% for hepatitis B (all p<0.001), from 79.9% to 85.7% for tetanus (p=0.041) and from 42.2% to 60.4% overall (p<0.001). Similarly, the vaccination coverage significantly increased for rheumatology patients, namely from 69.3% to 78.3% for influenza, from 34.5% to 85.0% for pneumococci, from 32.8% to 36.5% for hepatitis B (all p<0.001), from 59.8% to 89.6% for tetanus (p=0.160) and from 21.9% to 32.6% overall (p=0.841). For patients with dermatological inflammatory conditions, vaccination coverage significantly increased from 60.5% to 81.6% for pneumococci (p=0.031) and from 47.1% to 55.3% for hepatitis B (p=0.002). Vaccination coverage for patients with dermatological inflammatory conditions decreased from 73.7% to 71.1% for influenza (p=0.116), from 79.4% to 65.8% for tetanus (p=0.374) and from 45.9% to 31.6% overall (p=0.482).
Conclusions: The suboptimal vaccination rate measured in 2018 and the COVID-19 pandemic stressed the importance of vaccination recommendations to patients and healthcare professionals. We here show that the implementation of a vaccination tool integrated in the electronic medical record of patients is correlated with a significant increase in specific vaccination rates and also in the total amount of IMID patients that were fully vaccinated according to guidelines.
1. Rahier JF, Magro F, Abreu C, et al. Second European evidence-based consensus on the prevention, diagnosis and management of opportunistic infections in inflammatory bowel disease. J Crohns Colitis. 2014;8:443–468.

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TYPE OF PATIENT EDUCATION IMPACTS THE WILLINGNESS TO SWITCH FROM AN IV TO SC OF A BIOLOGICAL IN PATIENTS WITH IBD: A MULTICENTRE, COMPARATIVE STUDY. K. Asnong (1), E. De Dycker (2), E. Hoefkens (1), P. Geens (2), N. Lembrechts (1), T. Lambrechts (2), I. Van De Schoot (1), A. Paps (2), L. Pouillon (1), S. Vermeire (2), P. Bossuyt (3), M. Ferrante (2) / [1] Imelda Hospital, Bonheiden, Belgium, Department of Gastroenterology, [2] University Hospitals Leuven, Belgium, Department of Gastroenterology and Hepatology, [3] Imelda Hospital, Bonheiden, Belgium, Department of Gastroenterology.

Introduction: Subcutaneous (SC) formulations of CT-P13 and vedolizumab (VED) are currently available as new treatment option for patients with inflammatory bowel disease (IBD). The decision to switch requires a shared decision making based on adequate education of the patient, to avoid negative outcomes due to a nocebo effect.
Aim: The aims of this study were (1) to evaluate the percentage of patients with IBD in favour of switching to SC formulations and (2) to compare two educational strategies.
Methods: This was a multicentre study in patients with IBD on maintenance intravenous (IV) CT-P13 or VED. Patients attending the infusion unit were invited to complete a survey exploring the willingness to switch to SC formulations. In centre A, all patients were informed on the new SC formulations and the accompanying care pathway by an information leaflet and a face-to-face interaction with the IBD nurse, prior to completing the survey. In centre B, patients on a minimal interval of q8w were digital invited to the same survey via the e-health application of the hospital. Demographics, patient reported outcomes, willingness to switch and reasons for IV vs. SC preferences were captured.
Results: In total, 447 (participation ratio 83.6%) patients completed the survey (m/f: 212/235; CD/UC/IBD-U: 275/161/11; median age 45 IQR 33-57; remission CD/UC: 75%/82%). Most patients were open to SC treatment (47% yes, 33% doubt, 20% no). The main driver to switch was an anticipated decrease in hospital visits (86%) and overall time gain (78%). The main reason to continue IV was fear of change (60%) and uncertainty in case of relapse after switch to a SC formulation (46%). In univariate analysis, the self-estimated compliance rate was associated with the willingness to switch (p<0.0001). To evaluate the impact of the approach in patient education between the two centres, we compared the subgroup of patients on ≥q8w interval with a dosing of 5-10mg/kg CT-P13 or 300 mg VED (n=335). The willingness to switch was higher after a face-to-face approach (centre A) compared to a merely digital approach (centre B; 53.9 % vs. 40.9 % p=0.038), although patients in centre B had a higher educational level (p=0.003), more prior experience with other IBD SC medication (p=<0.001), lived further from the hospital (p<0.001) and had a younger age at diagnosis (p=0.019).
Conclusions: In this multicentre comparative study exploring the willingness to switch from IV to SC maintenance therapy with CT-P13 and VED, the majority is open to switch to a SC formulation. The direct approach and education of the patient by the IBD nurse impacts significantly the willingness to switch. In a follow-up we will investigate the actual switch rates.

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MICROBIOTA, NOT HOST ORIGIN DRIVES EX VIVO EPITHELIAL RESPONSE IN ULCERATIVE COLITIS PATIENTS AND NON-IBD CONTROLS. K. Arnauts (1), P. Sudhakar (2), S. Verstockt (2), C. Lapierre (2), S. Potche (2), C. Caenepeel (2), B. Verstockt (2), J. Raes (3), S. Vermeire (2), J. Sabino (2), C. Verfaillie (4), M. Ferrante (2) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of

Chronic Diseases, Metabolism and Ageing, [2] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing (CHROMETA), [3] KUL - University of Leuven, Leuven, Belgium, Department of Microbiology and Immunology, Rega Institute, [4] KUL - University of Leuven, Leuven, Belgium, Department of Development and Regeneration, Stem Cell Institute Leuven (SCIL).

Introduction: Host-microbial interactions in inflammatory bowel disease (IBD) are poorly understood. Furthermore, patients with IBD have microbial dysbiosis and their epithelial cells exhibit intrinsic defects.
Aim: We aimed to unravel the effect of exposure to microbiota on epithelial cells from both patients with ulcerative colitis (UC) and non-IBD controls.
Methods: Confluent Transwell® organoid-derived monolayers of 8 UC patients and 8 non-IBD controls were co-cultured for 6 hours with microbiota (3.108 cells) derived from active UC patients (n=3, endoscopic Mayo score ≥2) or healthy volunteer (HV, n=1, selected on high microbial cell count and presence of selected phyla1). For this purpose, fresh faecal samples were filtered and frozen in 0.9% NaCl. Inflammation was re-induced with 100 ng/ml TNF-α, 20 ng/ml IL-1β, and 1 µg/ml flagellin in confluent Transwell® cultures, 24 hours prior to microbiota co-culture. Transepithelial electrical resistance (TEER), 4 kDa fluorescein isothiocyanate (FITC) dextran (2 mg/ml) measurements, and RNA sequencing by Truseq were performed on epithelial cells, and 16S rRNA sequencing on microbiota samples before and after co-culture.
Results: The transcriptomic response of epithelial cells to microbiota was clearly influenced by the type of microbiota stimulation (no, UC or HV microbiota). However, this response was not influenced by the origin of the epithelial cells (UC or non-IBD controls. TEER and FITC dextran measurements showed a strong decrease in epithelial integrity (in both UC and non-IBD epithelium) following stimulation with UC microbiota, in contrast to HV microbiota. In UC epithelial cells, stimulation with microbiota from UC patients induced a stress phenotype including activation of EGR1 signalling, AP-1 family, FOSL genes, MAPK and JNK signalling. Activation of stress pathways (MAPK family cascades) and key markers (e.g. FOSB, FOSL1, MYC, EGR1, ATF3, NOTCH1) was lower after HV microbiota stimulation. Expression levels of key markers were UC microbiota specific and similar in epithelial cells of UC and non-IBD controls.
Conclusions: Not the host (UC vs non-IBD epithelial cells) but the microbial donor (UC vs HV) is driving the transcriptomic response. Epithelial cells from UC patients did not show an increased sensitivity towards microbiota stimulation compared to non-IBD epithelial cells. In contrast, exposure of epithelial cells to UC microbiota was sufficient to induce a strong stress response and barrier disruption. Further research on therapies to restore the microbial balance, to remove the constant trigger of dysbiosed microbiota, is required. 1.Vermeire, JCC, 2015

STANDARDIZED FECAL MICROBIOTA TRANSPLANTATION INCLUDING MICROBIAL BASED DONOR SELECTION IN ACTIVE ULCERATIVE COLITIS PATIENTS: A RANDOMIZED, PLACEBO CONTROLLED CLINICAL TRIAL. C. Caenepeel (1), S. Deleu (1), K. Arnauts (1), J. Vazquez Castellanos (2), S. Braekeleire (1), K. Machiels (1), F. Baert (3), F. Mana (4), L. Pouillon (5), P. Hindryckx (6), T. Lobaton (6), E. Louis (7), D. Franchimont (8), M. Ferrante (1), J. Sabino (1), S. Vieira-Silva (2), G. Falony (2), J. Raes (2), S. Vermeire (9) / [1] KUL - University of Leuven, Leuven, Belgium, Department of chronic diseases and metabolism, [2] Rega institute, Leuven , Belgium, Department of Microbiology and Immunology, [3] AZ Delta, Roeselare, Belgium, Department of gastroenterology and hepatology, [4] University hospitals Brussel, Jette, Belgium, Department of gastroenterology and hepatology, [5] Imelda Hospital, Bonheiden, Belgium, Department of gastroenterology and hepatology, [6] University Hospital Ghent (UZ Gent), Gent, Belgium, Department of gastroenterology and hepatology, [7] CHU of Liège, Belgium, Department of gastroenterology and hepatology, [8] Erasme Hospital, Brussels, Belgium, Department of gastroenterology and hepatology, [9] KUL - University of Leuven, Leuven, Belgium, Department of gastroenterology and hepatology.

Introduction: Four randomized controlled trials studying fecal microbiota transplantation (FMT) in active ulcerative colitis (UC) patients showed variable success rates. The efficacy of FMT appears to be influenced by various factors including donor- and procedure-specific characteristics.
Aim: We hypothesized that the outcome of FMT in patients with active UC could be improved by donor preselection on microbiota level, by using a strict anaerobic approach, and by repeated FMT administration.
Methods: The RESTORE-UC trial (NCT03110289) was a national, multi-centric double-blind, sham-controlled randomized trial. Active UC patients (Total Mayo score 4-10 with endoscopic sub-score > or = 2) were randomly allocated (1:1) to receive 4 anaerobic-prepared superdonor (S) FMT or autologous (A) FMT by permutated blocks (2-4) and stratified for weight, concomitant steroid use, and therapy refractoriness. S-FMTs were selected after a rigorous screening excluding samples with Bacteroides 2 enterotype, high abundances of Fusobacterium, Escherichia coli and Veillonella and the lowest microbial loads (Q1). A futility analysis after 66% (n=72) of inclusions was planned per protocol including a modified intention-to-treat (mITT) analysis using non-responder imputation (NRI) for patients receiving at least one FMT. The primary endpoint was steroid-free clinical remission (Total Mayo ≤ 2, with no sub-score >1) at week 8. Secondary outcomes included steroid-free PRO-2 remission (Combined Mayo subscores of ≤1 for rectal bleeding plus stool frequency) and response (≥3 points or/and ≥50% reduction from baseline in combined Mayo subscores for rectal bleeding plus stool frequency) and steroid-free endoscopic remission (Mayo endoscopic subscore ≤1) and response (Mayo endoscopy subscore ≤1 and ≥1 point reduction from baseline).
Results: Between March 2017-2021, 72 patients signed the ICF and 66 were randomly allocated to S-FMT (n=30) or A-FMT (N=36) and received at least one FMT. Both study arms were matched for baseline characteristics, yet a trend (p= 0,07) towards higher concomitant biological use in the S-FMT arm was observed. A remarkably high proportion of patients were previously exposed to biologicals (58.3% and 60.0% for the A-FMT and S-FMT group respectively). In the S-FMT and the A-FMT respectively 4 and 5 patients terminated the trial early due to worsening of colitis (4 in both arms) or FMT enema intolerance (1 A-FMT). They were included in the mITT analysis using NRI, showing after 66% of intended inclusions, the primary endpoint was reached in 3/30 (mITT with NRI 10.0%) S-FMT and 5/31 (13.9%) patients randomized to A-FMT (p=0.72). As the predefined minimum difference of 5% between both treatment arms was not attained, the study was stopped due to futility. Steroid-free PRO-2 remission was achieved in 7/30 (23,3%) patients on S-FMT and 10/36 (27,8%) on A-FMT (p= 0,78). Steroid-free PRO-2 response was attained by respectively 9/30 (30,0%) patients in the S-FMT arm and 12/36 (33,3%) patients in the A-FMT arm (p= 0,80). Steroid-free endoscopic response and remission were noted in 5/30 (16,7%) assigned to the S-FMT arm compared with 7/36 (19,4%) allocated to the A-FMT arm (p= 1.0). Of note, no patients on concomitant biologicals reached the primary endpoint, and there were 2 serious adverse events in the A-FMT arm: dysuria requiring hospitalization and worsening of UC requiring colectomy.
Conclusions: In this double-blind sham-controlled trial comparing repeated administrations of anaerobic-prepared S-FMT with A-FMT in patients with active UC, no significant difference in steroid-free remission rates at week 8 were observed. The FMT procedure was generally well tolerated, and no new safety signals were observed.

HIGH ACETATE CONCENTRATION REDUCES INFLAMMATION IN ORGANOID-DERIVED EPITHELIAL MONOLAYER FROM PATIENTS WITH ULCERATIVE COLITIS. S. Deleu (1), K. Arnauts (1), K. Machiels (1), G. Huys (2), J. Thevelein (3), J. Raes (2), S. Vermeire (1) / [1] KUL - University of Leuven, Leuven, Belgium, Chronic Diseases, Metabolism & Ageing (CHROMETA), TARGID, [2] KUL - University of Leuven, Leuven, Belgium, Microbiology and Immunology, [3] Erasmus High School, Brussels, Belgium, NovelYeast bv, Open Bio-Incubator.

Introduction: Short-chain fatty acids (SCFA), such as acetate and butyrate, have gained increasing interest for their potential to suppress IBD inflammation (1,4). Most data have been generated for butyrate, showing beneficial effects on the gut microbiome composition, intestinal barrier function and immune system (1). The effects of acetate are less known, despite its lower toxicity on epithelial cells and its ability to support growth of butyrate-producing bacteria by metabolic cross-feeding (2). Furthermore, the probiotic effect of the biotherapeutic yeast Saccharomyces cerevisiae var. boulardii might be linked to its high acetic acid production (3).
Aim: Here, we studied the effect of acetate on inflammatory markers and barrier integrity using an organoid-derived epithelial monolayer system obtained from Ulcerative Colitis (UC) patients.
Methods: Confluent Transwell® organoid-derived monolayers evaluated by Transepithelial electrical resistance (TEER) of 8 UC patients were basolaterally stimulated with control medium (CTRL) or with control medium containing an inflammatory mix (INFL) [100 ng/ml TNF-α, 20 ng/ml IL-1β, 1 µg/ml Flagellin]. After 24h, the monolayer was stimulated apically with CTRL or with control medium including a high acetate (HA) concentration [100mM] and TEER was measured at 0, 24, and 48h post-stimulation. After 48h, RNA extraction of the epithelial cell monolayers and qPCR for selected target genes (IL8, TNFα, CLDN1, CLDN2, HIF1A, ZO1, OCLDN, MUC2 and MKI67) was performed. Cytokine measurement was performed using Mesoscale Discovery (Proinflammatory panel 1) on apical and basolateral media. Data were analyzed using GraphPad Prism 9 (D'Agostino & Pearson test for normality followed by Wilcoxon tests).
Results: Transcriptomic analysis of the monolayer cells showed a decrease in expression of IL8 (p=0.03), TNFα (p=0.08) and increase of HIF1A (p=0.03) upon HA administration in inflamed conditions whereas the proliferation marker MKI-67 was upregulated (p=0,03). Moreover, these findings were supported by significant decreases in pro-inflammatory cytokines measured apically after HA stimulation such as IFNγ, TNFα, IL6, IL8 and IL1β (all p=<0.01). Basolaterally, IL8 (p=0.02) and IL13 (p=<0.01) increased significantly upon HA stimulation. Administration of HA was associated with a numerical though non-significant increase in TEER-values (p=0.15) suggesting a potential for improved barrier integrity.
Conclusions: In this UC patient-derived epithelial cell culture model, high acetate administration positively affected barrier integrity gene expression and TEER-values and suppressed expression and production of pro-inflammatory cytokines. References: 1. Venegas, 2019 2. Gill, 2018 3. Offei, 2019 4. Deleu, 2021.

PREDICTIVE MODELS FOR ASSESSING THE RESPONSE TO USTEKINUMAB IN CROHN'S DISEASE PATIENTS. A. Hubert (1), J. Toubeau (1), J. Bottieau (1), D. Franchimont (2), F. Vallée (1), C. Liefferinckx (2) /

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Introduction: The loss of response to biologics remains a clinical challenge for whom the discovery of predictive factors is helpful. In this direction, exploiting tree-based models on top of logistic regression (LR) allows to uncover unexpected valuable predictors.
Aim: The aim of the study is to develop performant predictions of ustekinumab (USK) response at one year of follow-up in a cohort of Crohn's disease (CD) patients using benchmark logistic regression (LR) and tailored tree-based techniques, Random forest (RF) and Gradient Boosting Decision Trees (GBDT).
Methods: This is a retrospective study based on a cohort of 80 CD patients treated with USK. Inputs include demographic data, disease characteristics as well as pharmacokinetics, clinical and biological parameters at baseline, week 8 and 16. After one-year follow-up, both clinical outcome (achieved in case of USK maintenance without optimization, n=80) and endoscopic outcome (achieved in case of remission/mild disease of SES-CD<10, n=52) are evaluated. The inputs are firstly ranked via the p-values for LR method and the impurity criterion for the tree-based ensemble methods. Then, the optimal subset of inputs for both methods is selected following a sequential feature selection. Due to the limited size cohort, a nested cross-validation framework was applied to avoid bias and overfitting. The performance of the final models is evaluated using the area under the ROC curve (AUC) with standard deviation (SD), sensitivity (Se) and specificity (Sp). All the analyses are performed with Python 3.6 using the packages statsmodels and Scikit-learn.
Results: Among the 80 CD patients included, 57.6% of patients had complicated phenotypes with 36.3% of B2 and 21.3% of B3. Also, 53.8% had a history of previous CD surgery. Only 10% of patients were naïve to biologic while 35% and 55% were previously exposed to one biologic and more than two biologics, respectively. Among the input data of interest, median USK trough levels were 6.5 µg/mL (3.3-9.3) at week 8 and 2.3 µg/mL (1.04-3.3) at week 16. At one-year follow-up, clinical and endoscopic outcomes were achieved in 56.2% (n=45/80) and 69% (n= 36/52), respectively. The predictive model characteristics were analyzed at the different timepoints of USK induction (baseline, week 8 and week 16). Whatever the outcome (clinical or endoscopic), predictive models exhibited an increased accuracy over the induction timepoints. Likewise, the three models (LR, FR and GBDT) exhibited a better accuracy by using the endoscopic outcome despite a lower number of available outcomes (n= 52) compared to clinical outcome (n=80). More specifically, at week 16, a multivariate LR allowed to predict endoscopic outcome with an AUC of 0.86 ± 0.12, Se 83% and Sp 70%. The explanatory variables selected by the model were CRP level at week 8 and 16, lymphocyte count at week 8 and USK trough levels at week 16. The best model to predict endoscopic outcome was obtained by RF with an AUC of 0.92 ±0.08, Se 91% and Sp 75%. The key inputs were lymphocyte count at baseline, lymphocyte and monocyte counts at week 8, and USK trough and CRP levels at week 16.
Conclusions: This study highlighted the complementary value of applying tree-based models on top of benchmark multivariate LR for the development of accurate predictive models. More specifically, the evolution of biological markers (such as the evolution of different leucocyte counts) during induction as well as USK trough levels at week 16 are relevant factors to predict endoscopic outcome among CD patients treated with USK.

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EXPERIENCE OF USING THE AUTOIMMUNE NUTRITION PROTOCOL IN PATIENTS WITH AUTOIMMUNE DISEASES OF THE DIGESTIVE TRACT.

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Introduction: Over the past few years, autoimmune pathology of the gastrointestinal tract has become much more common. Of course, this is due to the increased interest of clinicians and progress in diagnostics. Of the most common variants, autoimmune gastritis, celiac disease, and chronic inflammatory bowel disease should be noted. In 30% of cases, in addition to autoimmune gastritis, there is another autoimmune pathology: vitiligo, autoimmune thyroiditis, psoriasis, etc. The body can produce antibodies both exclusively against the parietal cells of the stomach and against the cells of the intrinsic factor. The result of such autoimmune reactions is hypoacid gastritis, multi-factor anemia, and malabsorption. The only treatment recommendation today is cyanocobalamin replacement therapy. Celiac disease is characterized by gluten intolerance, which is manifested by atrophic changes in the small intestine, which also leads to multifactorial anemia, malabsorption, malnutrition, impaired adaptation, and skin syndrome. The basis of treatment is the use of a gluten-free diet. In severe cases, it is possible to use glucocorticosteroids and immunosuppressants, to use a balanced enteral nutrition. Chronic inflammatory bowel diseases (ulcerative colitis, Crohn's disease) are idiopathic gastrointestinal disorders with a predominant autoimmune component. Due to the constant inflammatory component, a gradual progression of pathology occurs and, in addition to damage to the digestive tube, it is often necessary to simultaneously compensate for the extraintestinal manifestations of the disease. Inflammatory bowel diseases lead to maldigestion, malnutrition, polyfactorial anemia. In addition to these disorders, there is compensation for the side effects of the main drugs for treatment. Within the framework of the clinical protocol, mesalazine drugs, immunosuppressants, glucocorticosteroids, as well as the use of targeted therapy are used for treatment.
Aim: As you can see, the main common manifestations of autoimmune diseases of the gastrointestinal tract are maldigestion, malnutrition and multifactorial anemia.
Methods: Currently, at the Center for Preventive Gastroenterology, patients are observed with autoimmune gastritis-56, celiac disease-24, Crohn's disease-17, ulcerative colitis-21. Treatment and observation of these patients is carried out within the framework of the clinical protocol in force in the Republic of Belarus, as well as the European recommendations (UEG, WGO),
Results: However, for 1 year, some patients (37 patients from the observation group) were offered the use of dietary recommendations within the framework of Autoimmune Nutrition Protocol (Paleo Diet). The essence of the recommendations is the exclusion of products containing gluten (products from wheat, rye, oats, barley), coffee, chocolate, alcohol. For short periods of time from 3 weeks to 3 months, dairy products, highly allergenic products (eggs, nuts, seafood), as well as nightshades and products containing lectins and phytic acid, which increase the permeability of the intestinal tube (legumes), were excluded from the diet in turn ... 34 patients (92%), while observing nutritional recommendations, subjectively noted an improvement in general well-being and stool stabilization. 18 people (49%) adjusted body weight to normal body mass index. 11 people (30%) during the year did not require symptomatic drug correction (enzyme preparations, B9, symbiotics). The same 34 people (92%) decided to adhere to such a nutritional protocol in the future.
Conclusions: The autoimmune nutrition protocol has sufficient efficiency in patients with autoimmune gastrointestinal pathology, is quite easy to use, contains recommendations on the main macro and micronutrients, and is inexpensive to use. These factors make it possible to recommend it to a wider range of patients with autoimmune pathology. In the future, it is planned to develop scales and questionnaires, according to an objective assessment, the effectiveness of this method.

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INFLIXIMAB RE-CHALLENGE: COULD IT BE AN OPTION IN REFRACTORY IBD PATIENTS?

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Introduction: Infliximab (IFX) is effective in the treatment of inflammatory bowel disease (IBD). However, primary non-response and secondary loss-of-response rates go up to 30-40% and intolerance may occur leading to treatment switch. Unfortunately, even with increased availability of new molecules, some patients remain refractory to all currently available medical options.
Aim: The aim was to assess the effect of IFX re-challenge in a real-life cohort of highly refractory IBD patients.
Methods: A retrospective observational study was set up to analyse the effect of IFX rechallenge in IBD patients previously treated with IFX and found refractory to other biologics. Cases between August 2018 and June 2021 with at least 6 months of follow-up (FU) were analysed. Clinical, biological (CRP and faecal calprotectin [FC]) and endoscopic response was evaluated, as well as adverse events (AE).
Results: Ten patients with refractory IBD were included (9 Crohn's disease [CD], 1 ulcerative colitis [UC]). The mean age was 34.2 years (SD 9.25), 6 (60%) patients were female. All patients previously failed at least 2 biologics, 4 (40%) patients previously received 3 biologics and 5 (50%) patients 4-5 biologics. Six patients had IBD-related surgery before IFX rechallenge. Reasons to stop previous IFX included: primary non-response (n=3), loss of response (n=2), infusion reaction (n=2), clinical remission (n=1) and paradoxical psoriasis (n=1). All patients had active disease at the start of IFX re-challenge. Median baseline CRP was 12.6 mg/L [IQR 4.9-24.1] and FC 396 mg/kg [IQR 64-2786.8]. IFX was started in combination with systemic steroids, immunosuppressants and ustekinumab in 50%, 70% and 10% of patients, respectively. Baseline endoscopy showed severe active disease in 7/8 patients. IFX re-challenge was discontinued after the second administration in 2/10, due to a severe allergic reaction despite premedication with antihistamines and corticosteroids (1 anaphylactic shock admitted to intensive care unit, fully recovered). IFX was continued in 8/10. After 6 months of treatment, 3/8 patients (37.5%) had a clinical response and 3/8 (37.5%) were in clinical remission; 2/8 (25%) were in corticosteroid-free remission. After 1 year of treatment, follow-up data was available for 7 patients of whom 2 (28.6%) had a clinical response and 3 (42.9%) were in corticosteroid-free clinical remission. At 6 months the median CRP dropped to 1.1 mg/L [IQR 0.9-5.3] and the FC to 58 mg/kg [IQR 5.8-441.5]. After 1 year of treatment the CRP remained low: 1.5 mg/L [IQR 0.9-7.0], the median FC was 204 mg/kg [IQR 86-340]. Endoscopic response was assessed in 6 patients between 6-12 months, of whom 5 (83.3%) had a response, no endoscopic remission was observed. At 1 year of follow-up, all patients (7/7) required intensified dosing (4-weekly). Adverse events, not in all cases attributed to IFX, included: disease flare-up requiring hospitalization (3/10), liver test abnormalities (1/10), new perianal abscess (1/10), subobstruction (1/10), C. difficile infection (1/10), EBV infection (1/10) and Addison crisis (1/10).
Conclusions: IFX re-challenge was efficient in inducing clinical and endoscopic response in this highly refractory IBD population. However, there is a non-negligible risk of AE including infusion reaction.

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SAFETY ANALYSIS OF FILGOTINIB FOR ULCERATIVE COLITIS: RESULTS FROM THE PHASE 2B/3 SELECTION STUDY AND PHASE 3 SELECTIONLTE LONG-TERM EXTENSION STUDY. S. Vermeire (1), M. Ferrante (1), S. Schreiber (2), M. Watanabe (3), C. Yun (4), Y. Zhou (5), S. Zhao (5), J. Hsieh (4), U. Moerch (6), G. Rogler (7), E. Loftus Jr (8) / [1] University Hospitals Leuven, Belgium, Department of Gastroenterology & Hepatology, [2] University Hospital Schleswig-Holstein, Germany, Institut für Epidemiologie, [3] Tokyo Medical and Dental University, Japan, Institute of Advanced Research, [4] Gilead Sciences, Inc., California, United States, Clinical Research, [5] Gilead Sciences, Inc., California, United States, Biostatistics, [6] Gilead Sciences Inc. Copenhagen, Denmark, Medical Affairs, [7] University Hospital of Zurich, Switzerland, Department of Gastroenterology & Hepatology, [8] Mayo Clinic College of Medicine, Minnesota, United States, Department of Gastroenterology & Hepatology.

Introduction: Filgotinib (FIL) is an oral preferential Janus kinase (JAK) 1 inhibitor in development for the treatment of inflammatory diseases. FIL for the treatment of moderately to severely active ulcerative colitis (UC) was evaluated in the phase 2b/3, double-blind, placebo (PBO)-controlled SELECTION study (NCT02914522) and its long-term extension (LTE) study (NCT02914535).
Aim: To report the safety results from the FIL UC program.
Methods: Patients received FIL 100 mg, FIL 200 mg or PBO (2:2:1) once daily orally for up to 11 weeks for induction (cohort 1). At week 11, FIL induction responders were rerandomized 2:1 to continue the same dose of FIL or receive PBO maintenance for 47 weeks (cohort 2). Week 10 non-responders and patients with worsening disease during the maintenance study were eligible for open-label FIL 200 mg in the LTE. Patients completing the maintenance study could continue blinded dosing in the LTE. Cohort 3 comprised cohorts 1 and 2 and the LTE. Exposure-adjusted incidence rates (EAIRs) and exposure-adjusted event rates (EAERs) per 100 patient-years (PYs) were calculated for treatment-emergent adverse events (AEs) by treatment group in cohorts 1 and 2 (EAIR) and cohort 3 (EAER).
Results: In cohort 1, 1069 patients received FIL and 279 patients received PBO; baseline characteristics were generally similar across treatment groups (overall mean age, 43 years; mean UC duration, 8.4 years; mean Mayo Clinic Score, 9.0). EAIRs for AEs of interest were similar across treatment groups in cohorts 1 and 2. Treatment exposure for PBO, FIL 100 mg or FIL 200 mg in cohort 3 (i.e. cohorts 1 + 2 + the LTE) was 318, 360 and 1207 PYs, and median treatment duration was 12, 11 and 67 weeks, respectively. EAERs for all infections were similar across treatment groups, the most common being nasopharyngitis. Opportunistic infections were rare. EAERs for serious infections were low across treatment groups (2.2 [PBO], 3.5 [FIL 100 mg], 2.2 [FIL 200 mg]), the most common being appendicitis. EAERs for herpes zoster (HZ) were low in all treatment groups (0.3 [PBO], 0.3 [FIL 100 mg], 1.8 [FIL 200 mg]). HZ infections were cutaneous only and only one was serious. EAIRs for all infections in cohorts 1 and 2 were generally numerically higher for both PBO and FIL in patients over (vs under) 65 years old and in those with (vs without) biologic treatment failure. One case of pulmonary embolism occurred with FIL 200 mg induction and three venous thrombosis cases occurred with PBO maintenance/LTE (cohort 3).
Conclusions: FIL was well tolerated in patients with UC. Aggregation of AEs typical for pan-JAK inhibition was not observed, consistent with preferential JAK-1 inhibition with FIL.

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CORTICOSTEROID-FREE REMISSION OF ULCERATIVE COLITIS WITH FILGOTINIB MAINTENANCE THERAPY: POST HOC ANALYSIS OF THE PHASE 2B/3 SELECTION STUDY.
S. Vermeire (1), M. Ferrante (1), E. Loftus Jr (2), B. Feagan (3), C. Yun (4), J. Hsieh (4), X. Liu (5), S. Zhao (5), U. Moerch (6), W. Sandborn (7), T. Hibi (8) / [1] University Hospitals Leuven, Belgium, Department of Gastroenterology & Hepatology, [2] Mayo Clinic College of Medicine, Minnesota, United States, Department of Gastroenterology & Hepatology, [3] Western University, ON, Canada, Gastroenterology, [4] Gilead Sciences, Inc., California, United States, Clinical Research, [5] Gilead Sciences, Inc., California, United States, Biostatistics, [6] Gilead Sciences Inc. Copenhagen, Denmark, Medical Affairs, [7] University of California San Diego, La Jolla, United States, Division of Gastroenterology, [8] Kitasato Institute Hospital, Japan, Center for Advanced IBD Research and Treatment.

Introduction: Filgotinib (FIL) is a once-daily, oral, preferential Janus kinase 1 inhibitor in development for the treatment of inflammatory bowel disease. FIL for the treatment of moderately to severely active ulcerative colitis (UC) was evaluated in the phase 2b/3 randomized, double-blind, placebo (PBO)-controlled SELECTION study (NCT02914522). Long-term use of corticosteroids (CS) is associated with significant side effects.
Aim: The aim of this post hoc analysis was to assess the CS-sparing effects of FIL in the SELECTION study.
Methods: Patients (18–75 years old) with moderately to severely active UC were randomized (2:2:1) to receive FIL 100 mg (n = 564), FIL 200 mg (n = 507) or PBO (n = 280) once daily orally for up to 11 weeks (induction study). At week 11, FIL induction responders were rerandomized 2:1 to continue their induction FIL dose or to receive PBO (maintenance study). CS use was kept stable up to week 14, at which point mandatory CS tapering occurred. CS could be resumed during the maintenance study; however, if the baseline CS dose was exceeded this was considered treatment failure. In this post hoc analysis, CS-free remission was defined as remission at week 58 (endoscopic subscore ≤ 1, rectal bleeding subscore = 0 and ≥ 1-point decrease in stool frequency subscore to achieve 0 or 1) without systemic or localized CS use that was indicated for UC in the previous 1, 3, 6 or 8 months.
Results: The baseline characteristics of patients in the maintenance study were similar across treatment groups. Of the 92 patients receiving CS at maintenance baseline (week 11; maintenance week 0) who received FIL 200 mg during the maintenance study, 25 (27%) were in remission at week 58 and had been continuously CS-free for at least the previous 6 months. The proportion of CS-free remitters for 1, 3, 6 and 8 months at week 58 was consistently higher in the FIL 200 mg group than with PBO. In patients taking CS at maintenance baseline who had continued CS-use post baseline, lower median prednisone dosing was observed with FIL 200 mg than with PBO throughout the maintenance study (maximum difference at week 34 [maintenance week 23]: 5.0 mg vs 13.8 mg). In SELECTION, a total of 199 patients received FIL 200 mg in the maintenance study, of whom 74 (37.2%) were in remission at week 58; of these 74 patients, 69 (93.2%) were continuously CS-free for at least the previous 6 months.
Conclusions: In this post hoc analysis of SELECTION maintenance study data, FIL 200 mg was effective in reducing and eliminating CS use through to week 58 in patients with moderately to severely active UC. The vast majority of patients taking FIL 200 mg who were in remission at week 58 had not taken CS in the previous 6 months.

- I27 -

RAPIDITY OF SYMPTOM IMPROVEMENTS DURING FILGOTINIB INDUCTION THERAPY IN PATIENTS WITH ULCERATIVE COLITIS: POST HOC ANALYSIS OF THE PHASE 2B/3 SELECTION STUDY. M. Ferrante (1), S. Vermeire (1), S. Danese (2), T. Hibi (3), T. Ritter (4), J. Dinoso (5), J. Hsieh (6), C. Yun (6), J. Zhang (7), S. Zhao (7), E. Loftus Jr (8), G. Rogler (9) / [1] University Hospitals Leuven, Belgium, Department of Gastroenterology & Hepatology, [2] Humanitas Clinical and Research Center, Italy, Inflammatory Bowel Disease Clinical and Research Unit, [3] Kitasato Institute Hospital, Japan, Center for Advanced IBD Research and Treatment, [4] GI Alliance, Texas, United States, Gastroenterology, [5] Gilead Sciences, Inc., California, United States, Medical Affairs, [6] Gilead Sciences, Inc., California, United States, Clinical Research, [7] Gilead Sciences, Inc., California, United States, Biostatistics, [8] Mayo Clinic College of Medicine, Minnesota, United States, Department of Gastroenterology & Hepatology, [9] University Hospital of Zurich, Switzerland, Department of Gastroenterology & Hepatology.

Introduction: Filgotinib (FIL) is a preferential Janus kinase 1 inhibitor in development for the treatment of inflammatory bowel disease. SELECTION was a phase 2b/3 randomized, double-blind, placebo (PBO)-controlled trial to evaluate FIL for the treatment of moderately to severely active ulcerative colitis (UC) (NCT02914522).
Aim: The aim of this post hoc analysis was to assess the speed of improvement in patient-reported outcomes (PROs) during FIL treatment.
Methods: Eligible patients who were biologic-naïve or -experienced were enrolled in induction study A or induction study B, respectively. In each study, patients were randomized 2:2:1 to receive FIL 100 mg, FIL 200 mg or PBO once daily orally for 10 weeks. In this post hoc analysis, data from daily patient diaries up to day 15 of induction, including Mayo stool frequency subscores (SF; range, 0 [normal] to 3 [≥5 stools/day more than normal]) and rectal bleeding subscores (RB; range, 0 [no blood] to 3 [passing blood alone]), were used to evaluate the proportion of patients achieving predefined subscores or subscore reductions.
Results: Induction studies A and B comprised 659 and 689 patients, respectively. Baseline characteristics were similar across treatment groups within induction study A and within induction study B. In induction study A, more patients treated with FIL 200 mg vs PBO reported a reduction in SF of ≥1 from baseline as early as day 6 (FIL 200 mg, 35.8%; PBO, 20.6%, $p<0.01$) and every day from day 10, and a reduction in RB of ≥1 from baseline as early as day 4 (FIL 200 mg, 36.9%; PBO, 23.7%; $p<0.01$) and every day from day 7. In induction study B, more patients treated with FIL 200 mg vs PBO reported a reduction in SF of ≥1 from baseline as early as day 2 (FIL 200 mg, 21.6%; PBO, 12.1%; $p<0.05$) and a reduction in RB of ≥1 from baseline as early as day 3 (FIL 200 mg, 29.5%; PBO, 17.6%; $p<0.01$). More patients receiving FIL 200 mg vs PBO achieved the composite score of RB=0 and SF≤1 as early as day 9 in induction study A (FIL 200 mg, 18.8%; PBO, 9.5%, $p<0.05$). More patients receiving FIL 200 mg vs PBO achieved the composite score of RB=0 and SF≤1 as early as day 7 in induction study B (FIL 200 mg, 10.7%; PBO, 4.2%, $p<0.05$).
Conclusions: In this post hoc analysis of induction study data from SELECTION, improvements in SF and RB were observed within the first week of therapy with FIL 200 mg, compared with PBO, in patients with moderately to severely active UC. These data demonstrate that FIL 200 mg has rapid onset of action, as assessed by PROs, in both biologic-naïve and biologic-experienced patients.

- I28 -

EARLY ACHIEVEMENT OF PARTIAL MAYO SCORE REMISSION AND IBDQ NORMALIZATION IN PATIENTS WITH ULCERATIVE COLITIS TREATED WITH FILGOTINIB IN THE PHASE 2B/3 SELECTION STUDY. M. Ferrante (1), S. Vermeire (1), A. Oortwijn (2), B. Feagan (3), C. Yun (4), J. Zhang (5), L. Peyrin-Biroulet (6), S. Danese (7) / [1] University Hospitals Leuven, Belgium, Department of Gastroenterology & Hepatology, [2] Galapagos BV, The Netherlands, Medical Affairs, [3] Western University, ON, Canada, Gastroenterology, [4] Gilead Sciences, Inc.,

California, United States, Clinical Research, [5] Gilead Sciences, Inc., California, United States, Biostatistics, [6] Nancy University Hospital, France, Inflammatory Bowel Disease Unit, [7] Humanitas Research Hospital, Italy, Inflammatory Bowel Disease Clinical and Research Unit.

Introduction: Treatment goals for ulcerative colitis (UC) include the induction and maintenance of steroid-free clinical remission. Partial Mayo Clinic Score (pMCS) can be assessed non-invasively and can be used to evaluate disease activity.
Aim: To assess pMCS remission in patients with UC treated with filgotinib (FIL), a once-daily, oral, Janus kinase 1 preferential inhibitor, in the SELECTION trial.
Methods: SELECTION was a phase 2b/3 double-blind, randomized, placebo-controlled trial comprising two induction studies and one maintenance study (NCT02914522). Adults (18–75 years) with moderately to severely active UC were randomized 2:2:1 to receive FIL 200 mg, FIL 100 mg or placebo (PBO) orally once daily for up to 11 weeks in Induction Study A (biologic-naïve patients) and Induction Study B (biologic-experienced patients). Patients who achieved clinical remission or MCS response at week 10 entered the 47-week Maintenance Study at week 11. Patients who received induction FIL were rerandomized 2:1 to their induction FIL regimen or PBO. PBO responders continued PBO. We assessed pMCS remission (pMCS $\leq$2 and no individual subscore >1) in patients treated with FIL 200 mg vs PBO at baseline and at predefined timepoints during the induction and maintenance studies using the Cochran–Mantel–Haenszel test with non-responder imputation. These were post hoc analyses, and hence all p values presented are nominal. The relationship between pMCS remission and Inflammatory Bowel Disease Questionnaire (IBDQ) score was assessed using concordance rate.
Results: At week 10, pMCS remission was achieved in a greater proportion of biologic-naïve (53.9% vs 31.4%, p<0.0001) and biologic experienced patients (33.2% vs 8.5%, p<0.0001) treated with FIL 200 mg than PBO. Differences between the FIL 200 mg and PBO group were observed as early as week 2 (biologic-naïve, 15.1% vs 8.0%, p=0.041; biologic-experienced, 10.3% vs 4.2%, p=0.027). A higher proportion of patients who continued FIL 200 mg than those who switched to PBO in the Maintenance Study were in pMCS remission 9 weeks after rerandomization (week 20: 67.8% vs 49.0%, p=0.001). During maintenance, the proportion of patients in pMCS remission remained relatively stable among those who continued FIL 200 mg compared with patients who switched to PBO, with 61.8% vs 26.5% (p<0.0001) in pMCS remission at week 58. Patients in pMCS remission were more likely to have an IBDQ score of $\geq$170 (indicative of remission) than those not in remission at week 10 (concordance rate 74.6%) and week 58 (concordance rate 83.7%).
Conclusions: FIL 200 mg induced pMCS remission as early as week 2, and a higher proportion of patients who received FIL 200 mg vs PBO in the Maintenance Study were in pMCS remission at week 58. Patients in pMCS remission reported better quality of life than those not in remission.

- I29 -

THE CLINICAL DECISION SUPPORT TOOL HAS LOW PERFORMANCE IN PREDICTING OUTCOME TO USTEKINUMAB IN CROHN'S DISEASE. D. Alsoud (1), J. Sabino (2), M. Ferrante (3), B. Verstockt (3), S. Vermeire (3) / [1] KUL - University of Leuven, Leuven, Belgium, Translational Research in Gastrointestinal Disorders, Department of Chronic Disease, Metabolism and Ageing, [2] University Hospitals Leuven, Belgium, Department of Gastroenterology and Hepatology, [3] University Hospitals Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Several biologicals and small molecules have been added to the therapeutic arsenal of inflammatory bowel disease, which generated a wide interest in precision medicine. In this context, both clinical features and laboratory tests have shown some correlation with therapy outcome. Recently, an online clinical decision support tool[1] (CDST) was built, using clinical and biochemical variables (e.g. disease location, prior anti-TNF exposure), to help physicians predict the outcome of various biological treatments in Crohn's disease (CD).
Aim: To evaluate the predictive performance of the clinical decision support tool in patients with CD initiating ustekinumab (UST).
Methods: Baseline data were collected from consecutive CD patients who started UST IV induction followed by eight weekly UST 90 mg SC maintenance from December 2015 through March 2021 at our referral center. The probability of achieving clinical remission (low, intermediate, or high) was determined using the online CDST using patients' data. Also, differences in rates of primary non-response and ustekinumab persistence were compared between CDST classifications. Primary non-response was defined as failing to attain endoscopic response ($\geq$50% decrease in SES-CD) nor clinical response (a drop in the physician global assessment score or patients reported outcome), both assessed at month 6 after UST initiation. Finally, we studied the relation between the individual components used to construct the CDST and the three classifications in a univariate analysis.
Results: A total of 291 CD patients started UST, of whom 237 had objectively-assessed (CRP, fCal, symptoms or endoscopy) baseline disease activity. Using the CDST, the proportion of patients with "low", "intermediate" or "high" probability to attain clinical remission were 11.8 % (n=28), 55.7 % (n=132) and 32.5 % (n=77), respectively. The CDST classifications ("low", "intermediate" and "high") could not discriminate patients with primary non-response (p value = 0.18), nor identify trends in drug persistence (p value = 0.44). In the univariate analysis, 3 out of 9 components (active fistulizing disease, disease location and concomitant immunomodulatory use) were not significantly contributing to the CDST classification.
Conclusions: The recently developed clinical decision support tool showed low performance in predicting short-term (primary clinical and endoscopic response) and long-term (drug persistence) real-life outcomes in CD patients starting UST. These findings underscore the necessity of incorporating molecular variables, in addition to clinical ones, to construct reliable and reproducible tools to predict therapeutic outcomes. 1. https://via.juxlyapps.com/pathway/archemedx/ibd-cdst/index.html#/disease-selection

- I30 -

ASSOCIATIONS OF BLOOD DERIVED IMMUNE CELL TRANSCRIPTIONAL SIGNATURES WITH DISEASE LOCATION IN IBD. P. Sudhakar (1), B. Verstockt (2), J. Cremer (3), S. Verstockt (1), J. Sabino (2), M. Ferrante (2), S. Vermeire (2) / [1] KUL - University of Leuven, Leuven, Belgium, TARGID, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [3] KUL - University of Leuven, Leuven, Belgium, Department of Microbiology and Immunology.

Introduction: Disease location is a prominent axis of heterogeneity in Inflammatory Bowel Disease (IBD) with many implications.
Aim: Using genome-wide profiling of the transcriptome of monocytes and CD4+ T cells isolated and purified from whole blood, we aimed to identify molecular signatures and mechanisms associated with different locations among IBD patients.
Methods: Blood was collected from 125 IBD patients (87 CD, 38 UC) with endoscopy-proven active disease (presence of ulcerations). Cell separation and fluorescence activated cell sorting were performed to separate the monocyte and CD4+ T cell fractions, from which RNA was subsequently isolated and sequenced (Illumina HiSeq 4000NGS). We used different supervised and unsupervised approaches (differential expression, pathway-based data integration, latent factor based models, regularized generalized canonical correlation analysis and co-expression networks) to interpret the differences in the gene expression datasets of monocytes and CD4+ T cells from patients with different disease locations (Montreal classification). Functional enrichment analysis was performed using the ReactomePA package. Regulatory relationships and therapeutic relevance information were retrieved from the ChEA3 and the OpenTargets resources respectively. Comparison with single-cell and bulk-derived gene expression signatures from other auto-immune diseases were performed using the ADEX resource.
Results: Highly variant disease-location (DL)-associated genes (FDR <= 0.1) in monocytes and CD4+ T cells were identified using latent factor based unsupervised models. These genes were known to be involved in IBD pathogenesis and/or intestinal inflammation. Additional supervised analysis revealed significant differences in CD4+ T cells between ileal CD patients and UC patients. RAF-independent MAPK-activation pathway and FOXO-mediated transcriptional pathway (downregulated in UC patients) were over-represented (FDR <= 0.05) among the features distinguishing ileal CD and UC patients based on signature sets derived from the above-mentioned multiple approaches. Of note was the finding that 12.5% of the DL associated co-expression modules were also annotated as IBD drug targets. Based on gene expression signature from bulk and single-cell sources, the DL associated genes were found to be active in many other auto-immune diseases such as rheumatoid arthritis, systemic sclerosis, Sjögren's syndrome, type 1 diabetes and Systemic lupus erythematosus, suggesting their role in mediating immune malfunctions.
Conclusions: We identified signaling pathways and transcription factors which could drive the expression differences observed in the circulating immune cells between ileal CD and UC patients.

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SURVEYING THE USE OF COMPLEMENTARY ALTERNATIVE MEDICINES AMONG IBD PATIENTS. P. Sudhakar (1), R. Stiers (2), E. De Dycker (2), P. Geens (2), A. Paps (2), T. Lambrechts (2), B. Keersmaekers (2), J. Sabino (3), M. Ferrante (3), S. Vermeire (3), B. Verstockt (3) / [1] KUL - University of Leuven, Leuven, Belgium, TARGID, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, TARGID, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Inflammatory Bowel Disease (IBD) is a chronic inflammatory disease of the gut, characterized by multiple symptoms of which some cannot be successfully managed by existing conventional therapies. The use of complementary alternative medicines (CAMs) and CAM services among patients with chronic disorders including IBD has increased globally over the past several years (Rawsthorne Gut 2012; Weizman APT 2012).
Aim: The main aims of this study were (a) to profile the use of CAMs and CAM services in a cohort of IBD patients being treated at a Belgian IBD referral center and (b) to identify the clinical and demographic factors associated with the use of CAMs.

Methods: An anonymized and customized Dutch version of the international questionnaire to measure the use of complementary and alternative medicine (I-CAM-Q – Quandt J Altern Complement Med 2009) was provided over an 8-week period spanning September and October 2021) to all IBD patients visiting the IBD outpatient clinic and infusion unit. Pearson's Chi-square test was used to identify the relationships between clinical and demographic variables (age, gender, educational status) and CAM usage.
Results: From among the 410 IBD (144 UC, 253 CD) patients who responded to the survey, 173 (42.2%) were using CAMs or had used CAMs. A vast majority (79.8%) of the CAM using IBD patients reported the use of nature-based therapies (aloe vera, green tea, curcumin, cannabis, vitamin/mineral supplements and probiotics), a fifth of which was accounted for by Cannabis and its derivatives. This was followed by mind-body therapies (42.1%) (mindfulness, yoga, acupuncture, hypnotherapy, meditation). Two-thirds of patients (66.7%) mentioned to use CAMs for IBD-related symptoms. 125/173 of the CAM using IBD patients attributed the use of CAMs to their know-how about the potential of CAMs in ameliorating symptoms (32%), low efficacy or presence of adverse effects of conventional therapies (29.6%), minimize disease burden (28.8%) and avoiding surgery (7.2%). A vast majority (93.9%) of the CAM using IBD patients who responded to the query stated that consultation with their gastroenterologist would be beneficial to ascertain possible interference with their ongoing conventional therapy.
Conclusions: A significant proportion of IBD patients use CAMs to manage the complicated and often systemic symptoms of IBD. The most frequently used CAMs included nature-based therapies such followed by mind-body medicine. Given that CAMs are not officially regulated as medicinal therapies, their impact on conventional therapies is not entirely clear and should be further studied. Multi-center surveys profiling the use of CAMs in IBD patients as well as other chronic disorders are warranted.

- I32 -

SUBCUTANEOUS INFLIXIMAB CT-P13 IN CLINICAL PRACTICE: A BELGIAN SINGLE CENTER EXPERIENCE. L. Cornelis (1), E. De Jonckere (1), J. Bossuyt (2), H. Vanpoucke (3), L. Desomer (1), D. De Wulf (1), F. Baert (1) / [1] AZ Delta, Roeselare, Belgium, Department of Gastroenterology, [2] AZ Delta, Roeselare, Belgium, Department of Data Management and Analytics, [3] AZ Delta, Roeselare, Belgium, Department of Laboratory Medicine.

Introduction: Subcutaneous (SC) infliximab CT-P13 (IFX) has recently been registered for the treatment of moderate-to-severe inflammatory bowel disease (IBD). The SC route is an attractive option for patients. However, many open questions remain on how to safely switch patients from maintenance IV to SC administration.
Aim: To assess switching from IV to SC Infliximab therapy in IBD patients through clinical and biochemical evaluation.
Methods: Starting April 2021 for ulcerative colitis (UC) and September 2021 for Crohn patients in durable remission (no symptoms, normal labs and calprotectin) on eight-weekly (or six-weekly) infliximab and therapeutic IFX trough level were offered the option to switch to SC therapy. All patients are monitored prospectively every 3 months with PRO's (with Awell app), labs including IFX concentrations and faecal calprotectin every 6 months. These data were added to our medical file system (HIX) and specific IBD database (URCARE).
Results: December 1, 53 (42% UC, 58% Crohn) of 127 IBD patients on IFX have chosen to switch to SC IFX therapy with 17 patients (100% UC, 0% Crohn) passing 3 months follow-up and 10 patients (100% UC, 0% Crohn) 6 months respectively (median follow-up 6.5 months for UC, 1 month for Crohn). Median body weight was 72 kg (range 52-105). 13 patients (25%) were on concomitant Azathioprine (4), Mesalamine (6), Beclomethasone (1) and Methotrexate (2). The UC cohort median age was 37 yrs (range 21-74), M:F ratio = 10:12, 86% proctitis, 55% left sided colitis and 27% pancolitis. The Crohn cohort median age was 39 yrs (range 18-70), M:F ratio = 17:14, 42% small bowel only, 19% colon only and 39% small bowel and colon. Hitherto all patients stayed into deep remission according to clinical Mayo score, CRP and calprotectin. Median (+SD) CRP, thrombocytes and calprotectin remained stable from at last IFX infusion to 3 months follow up (1.2±9.2 vs. 1.3±1.6 mg/dL; 240±70 vs. 258±57 x10^3/µL) and 6 months follow up (1.2±9.2 vs. 1.4±2.0 mg/dL; 240±70 vs. 275±60 x10^3/µL; 40±446 vs. 20±470 mcg/g). The median (+SD) IFX serum concentration at month 3 doubled compared to the concentration with IV therapy (12.0±1.5 vs. 4.8±2.8 mg/L) and stayed stable over time (at 6 months 11.8±3.8 mg/L). Local pain and injection site reactions were reported in 41% and 23% of patients respectively. All patients continued SC treatment without request to switch back to IV.
Conclusions: Switching UC and Crohn patients in deep remission and adequate trough levels from maintenance IV tot SC infliximab therapy was successful short term. A proportion of patients experienced pain and or injection site reactions. Results will be updated at the meeting.

BELGIAN SOCIETY FOR PAEDIATRIC GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION (BESPGHAN)

- K01 -

THE THREAT OF ACCIDENTAL SUPERMAGNET INGESTIONS. P. Alliet (1), E. Janssens (1) / [1] Jessa Hospital, Hasselt, Belgium, Department of Paediatrics.

Case Report: An 18-month-old boy was sent to the Emergency Room because of persistent vomiting. The evening before he enjoyed a heavy meal to celebrate the end of the Ramadan period. The clinical examination was without particularities, except for a runny nose. The diagnosis of indigestion or (viral) gastritis was made. Patient was sent home. He was represented at the ER five days later. He stopped vomiting for 3 consecutive days after his first hospital visit, but started to vomit again the last 2 days, the last night even two times with bilious vomiting. His appetite was decreased since one week. The infant was not comfortable during abdominal palpation. An abdominal ultrasound showed air superposition in the epi- and mesogastrium. Due to that reason the position of the arteria/vena mesenterica posterior could not be checked. There were no signs of intersusception. An abdominal X-ray showed a corpus alienum, presumably magnets, in the mesogastrium and free air under the right diaphragm. An abdominal CT-scan could not visualise whether the magnets were situated in or outside the intestinal lumen. At laparoscopy, clitted small intestinal loops due to the magnet bullets with multiple perforation sites were detected as well as a purulent peritonitis in the left fossa iliaca. Magnets were removed. Perforations were sutured. Postoperatively augmentin was given. Patient recovered completey. Neodymium supermagnets (SREM) were first introduced in 2009, marketed as stress relieving desk toys, intended for consumers above the age of 14 years. Despite public education campaigns the increased sale coincided with a significant increase of accidental magnet ingestions in children of all ages. When more than one SREM is ingested, they tend to attach across the bowel loops, cut off vascular supply, leading to tissue perforation, fistulae, sepsis or death. In 2012 an action from NASPGHAN and the AAP towards the Consumer Products Safety Commission led to a ban of the high-powered magnet sets, which leaded to a prompt decrease in accidental pediatric magnet ingestions. The industrial lobby sued the CPSC after which they could be sold again with as result a new increase in accidental magnet ingestions. After documenting the rise in accidental ingestions by a good survey, a new legislative initiative "Magnet Injury Prevention Act" led to a commercial ban of these magnets in the US. A similar initiative should be undertaken in Belgium and Europe.

- K02 -

AN UNUSUAL RECTAL PROTRUSION IN A TWO-YEAR-OLD GIRL CAUSED BY A RECTAL DUPLICATION CYST: CASE REPORT AND LITERATURE REVIEW. E. Levy (1), Y. Vandenplas (2), K. Huysentruyt (2), B. Hauser (2), C. Vercauteren (3), K. Vanderlinden (3), E. De Greef (2), D. Vervloessem (4), T. Devreker (2) / [1] CHU Saint-Pierre, Brussels, Belgium, Pediatric gastroenterology, [2] UZ Brussel, Jette, Belgium, KidZ Health Castle, paediatric gastroenterology, [3] UZ Brussel, Jette, Belgium, KidZ Health Castle, department of Surgery - Paediatric Surgery, [4] ZNA Antwerpen, Antwerpen, Belgium, department of Surgery - Paediatric Surgery, Saffier network.

Introduction: The most frequent cause of rectal prolapse in young children is constipation (55%). Combined anatomic and neurologic abnormalities are reported to occur in 10% of the cases. A duplication cyst as cause of rectal prolapse is rare. A duplication cyst is a congenital anomaly of unknown aetiology, formed around the 1st or 2nd month of embryonic development. How to approach these patients in the clinic in not always easy due to the slightly different presentation of symptoms and young age.
Aim: Presenting a rare case of unusual rectal protrusion in a two-year-old girl, caused by a rectal duplication cyst. We also have evaluated the literature about diagnosis and management.
Methods: The case information was retrieved from hospital reports. We used heading and key words of interest to extract articles in English language from PubMed and Google Scholar. Interesting references in included articles were also considered.
Results: We present a case of a two-year-old girl with a unusual rectal protrusion, occurring four months after starting toilet training. The rectal protrusion could be manually repositioned. Digital rectal exam was normal, as the rest of the physical examination. The initial diagnosis was a prolapse related to constipation. An ultrasound of the abdomen was normal. Due to parental observation and pictures of deformation of the stools, a polyp was suspected. However, colonoscopy was normal with however an impression of a slight bulging of the mucosa in the rectum. A contrast radiography with gastrographin enema did not show any abnormality. A magnetic resonance imaging of the abdomen was performed and showed a suspicion of a lipoma (10 x 19 x26 mm) pre-sacral against the rectum wall. Multidisciplinary approach was performed with additional advice of paediatric neurologist, radiologist and surgeons. Additional blood/urine investigation was performed (catecholamines in urine, general blood analysis including alpha-fetoprotein and human chorionic gonadotropin) and was normal. A surgical intervention was performed: through a posterior sagittal incision the prerectal mass could be completely removed out of the posterior rectal wall. Pathology result showed a

duplication cyst, completely excised. After surgery, the rectal protrusion did not recur during a three-month follow-up. We found three other case reports mentioning rectal duplications cysts presenting with a rectal prolaps. However, they had additional clue-symptoms compared to our case like a palpable mass during digital rectal examination and/or rectal bleeding. Literature review shows different diagnostic approaches. For the management of a rectal duplication cyst, a minimal invasive surgery with total excision by a posterior sagittal approach is suggested.
Conclusions: A duplication cyst can be a rare cause of rectal protrusion in young children. Parental documentation and a multidisciplinary approach were key in finding the correct diagnosis, after a normal digital rectal exam led us astray. Diagnostic strategies vary in the literature.

- K03 -

COVID-19 PANDEMIC IMPACT: DELAY IN PRESENTATION AND ALTERED DISEASE COURSE IN CHILDREN WITH GASTROINTESTINAL AND HEPATIC DISORDERS IN A TERTIARY CARE CENTER. A. Ravindranath (1), R. Wadhwa (2) / [1] Apollo BGS Hospital, Mysore, India, Pediatric Gastroenterology, [2] Apollo BGS Hospital, Mysore, India, Gastroenterology.

Introduction: The ramifications of COVID-19 extend beyond direct infection with SARS-CoV2. Disruption in access to healthcare has resulted in delayed diagnosis and treatment for several diseases other than those due to COVID-19. No previous study has systematically analyzed the effect on children with gastrointestinal and hepatic disorders.
Aim: The aim of this study is to systematically analyze the impact of COVID-19 pandemic in delaying presentation to pediatric gastroenterology service and its effect on disease course.
Methods: All children presenting to a tertiary pediatric gastroenterology unit (September 2020-May 2021) were screened. Children who delayed presentation by at least 2 weeks after referral by primary pediatrician or missed their follow-up visit by more than 2 weeks due to reasons directly or indirectly related to COVID-19 pandemic were included. Demographic and clinical details were recorded. They were managed as per routine recommendations. Reasons for delayed presentation were noted after interviewing parent or guardian.
Results: Out of 450 children who presented to out-patient department, 47 (25 boys) aged 64 months (2-204) had delayed presentation. 14/47 were already on follow-up and 33/47 were new cases. The mean delay in presentation after being referred was 9.2 months (1 to 24). 30/47 (64%) were from rural and 17/47 (36%) were from urban areas. The following were the direct consequences of delayed presentation: Six died (biliary atresia,n=3; Wilson disease,n=1; fatty-acid-oxidation-defect,n=1; giant cell hepatitis with hemolytic anemia,n=1); 7 were severely malnourished (Crohn's disease,n=4; cow's milk protein allergy (CMPA),n=3), missed diagnosis [recurrent acute pancreatitis (n=2) were treated as gastritis, mesenteric cyst (n=1) as abdominal tuberculosis], dietary non-compliance (CMPA,n=6; lymphangiectasia,n=1), non-compliance to medications [cyclical vomiting syndrome,n=1 (recurrence of symptoms); progressive familial intra-hepatic cholestasis,n=2 (persistent pruritus), glycogen storage disease,n=2 (recurrent hypoglycemia)]; treatment with native medications (systemic mastocytosis, n=1; solitary rectal ulcer syndrome, n=2; Neiman Pick Type C, n=1). Reasons for delayed presentation were: transport restrictions due to lockdown (n=15), fear of contracting COVID in a tertiary hospital (n=26) and loss of income (n=6).
Conclusions: 10% children with gastrointestinal and hepatic problems delayed presenting by 9.2 months due to COVID-19 pandemic. 12% of them died due to treatable causes.

BELGIAN GROUP FOR DIGESTIVE ONCOLOGY (BGDO)

- O01 -

THERAPEUTIC YIELD OF COMPREHENSIVE MOLECULAR PROFILING IN CHOLANGIOCARCINOMA: A RETROSPECTIVE SINGLE CENTER STUDY. J. Vancanneyt (1), B. Wilmsen (1), C. Luyten (1), C. Verslype (1), E. Van Cutsem (1), T. Roskams (2), S. Tejpar (1), I. Vanden Bempt (3), J. Dekervel (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Pathology, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Genetics.

Introduction: Cholangiocarcinomas (CCAs) are rare and highly heterogeneous biliary malignant tumors that can arise at any site of the biliary tree. Each subtype (intrahepatic (iCCA), perihilar (pCCA) or distal (dCCA)) has a distinct epidemiology, biology, prognosis and strategy for clinical management. For patients with locally advanced or metastatic disease, the available systemic therapies are of limited effectiveness. In recent years, the introduction of next-generation sequencing (NGS) technologies opened new horizons for a better understanding of the genetic pathophysiology of CCA and consequently, for the identification of molecular alterations for targeted treatments.
Aim: The aim of this study was to identify the proportion of targetable alterations found in cholangiocarcinoma and to study the effect of targeted treatment on disease control.
Methods: We retrospectively collected the results of comprehensive genomic testing obtained in patients with locally advanced or metastatic cholangiocarcinoma in a single center between 1/12/2018 and 16/9/2021. Genetic profiling of the tumor was either done by in-house testing (SeqCap NGS, microsatellite instability (MSI) immune histochemistry (IHC), HER2 IHC and in-situ hybridization) or by FoundationOne CDx/FoundationOne Liquid CDx. Genomic findings were classified using the ESMO Scale for Clinical Actionability of molecular Targets (ESCAT).
Results: 125 patients were included with a median age at diagnosis of 65 years. Male/female proportion was 64/61 (51,2%/48,8%). Four patients had underlying primary sclerosing cholangitis (PSC). In-house testing was performed in 41 patients, FoundationOne CDx in 57 and FoundationOne Liquid CDx in 21 patients. 5 samples failed quality control. All subtypes of biliary tumors were included: 6 gallbladder cancers (4,8%), 1 mixed hepatocellular carcinoma/cholangiocarcinoma (0,8%), 65 iCCAs (51,2%), 32 pCCAs (26,4%), 19 dCCAs (15,2%), 1 ampullar carcinoma (0,8%) and 1 carcinoma of unknown primary with histologic features of CCA (0,8%). Class 1 alterations, defined as druggable in clinical routine, were found in 22,7% of patients and consisted of MSI-H (6,7%), FGFR2 fusions (9,1%) and IDH1 mutations (10,1%). NTRK fusions were not detected. 30 % of patients had a class 2 alteration (druggability under investigation) including MSS/TMB-high (2,3%), mutations in BRCA1 (2,0%), BRCA2 (3,0%), CHEK2 (3,0%), PALB2 (1,0%), ATM (4,0%), AKT1 (1,0%) or PIK3CA (8,1%), ROS rearrangement (2,0%), BRAF V600E mutations (2,0%), MET amplification (1,3%) and HER2 amplification (7,0%). 28,0 % and 20,0 % of patients with a class 1 and class 2 alteration respectively were treated with targeted treatment. With a median follow-up of 5,4 months, the median PFS on this targeted treatment was not yet reached.
Conclusions: In this large single center cohort, comprehensive molecular characterization led to the identification of targetable and potentially targetable alterations in a significant proportion of patients with locally advanced or metastatic CCA. Given the emergence of new targeted drugs and the limited effectiveness of standard chemotherapy, molecular analysis should be considered in all patients fit enough for systemic treatment.

- O02 -

DETERMINATION OF THE HISTOLOGICAL GROWTH PATTERNS OF COLORECTAL PERITONEAL METASTASES AND EVALUATION OF THEIR PROGNOSTIC IMPACT. A. El Asmar (1), P. Demetter (2), F. Fares (3), F. Sclafani (4), A. Hendlisz (5), D. Larsimont (2), V. Donckier (1), G. Liberale (1) / [1] Institut Jules Bordet, Brussels, Belgium, Surgical Oncology, [2] Institut Jules Bordet, Brussels, Belgium, Pathology, [3] Université Libre de Bruxelles, Belgium, Surgery, [4] Institut Jules Bordet, Brussels, Belgium, Oncology, [5] Institut Jules Bordet, Brussels, Belgium, Gastroenterology Oncology.

Introduction: Metastatic colorectal cancer (CRC) constitutes one of the leading causes of cancer-related deaths worldwide. 20% of patients with CRC will ultimately develop peritoneal metastasis (PM). Cytoreductive surgery (CRS) +/- HIPEC remains the standard and only potential curative treatment for PMCRC, in a selected number of patients. However, we are still lacking more accurate prognostic factors for these patients. Many studies have demonstrated that the histopathological growth pattern (HGP) of colorectal hepatic metastases (HM) is a major prognostic factor. Patients with HM and a desmoplastic growth pattern, had a better prognosis in terms of overall survival (OS), and disease-free survival (DFS), when compared to the non-desmoplastic group. However, histological growth patterns had never been analyzed in peritoneal metastases of CRC origin (PMCRC).
Aim: In this study, we aimed to identify and describe reproducible HGPs in PMCRC, and to assess their potential correlation with DFS and OS.

Methods: This is a retrospective study including all patients operated for PM of colorectal origin between July 2012 and March 2019 with a PCI ≤ 6. The completely excised peritoneal nodules, were included for each patient, and all of the pathology slides showing the margins between the metastatic nodule and the peritoneum were analyzed. The pathologist estimated, for each block reviewed, the relative presence (in percentage %) of the distinct HGP, at the tumor-peritoneal interface. The mean HGP score was then calculated in each patient. DFS and OS were calculated with the KM method and difference between groups were analyzed with the log Rank test.
Results: In this cohort, 50 patients met the inclusion criteria and histological slides from 38 patients were available for analysis. We identified a dominant "pushing" type (≥ 60%) in 16 patients (42%), and a dominant "infiltrating" type (≥ 60%) in 22 patients (58%). No desmoplastic HGP were found. Patients operated for PMCRC, showing a dominant "Infiltrating HGP", have a worse prognosis compared to patients with a dominant "Pushing HGP", in terms of DFS (19.5 vs 73.2 months respectively; p=0.043) and OS (51.3 vs 102.6 months respectively; p=0.044).
Conclusions: In this study, 2 histological growth patterns have been reproducibly identified in patients operated for Peritoneal metastases of colorectal origin: the "pushing" type and the "infiltrating" type. A dominant Infiltrating-HGP is associated with worse DFS and OS.

- O03 -

HOMOGENEITY OF PATHOLOGICAL RESPONSE AND HISTOPATHOLOGICAL GROWTH PATTERN IN RESECTED COLORECTAL LIVER METASTASES IS ASSOCIATED WITH FAVORABLE SURVIVAL OUTCOME AFTER SURGERY. P. Baldin (1), G. Beniuga (2), J. Carrasco (3), A. De Cuyper (4), I. Sinapi (5), C. Hubert (6), B. Navez (7), M. Castella (8), A. Van Maanen (9), B. Mlecnik (10), A. Jouret-Mourin (2), M. Van Den Eynde (11) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Pathology, [2] IPG, Charleroi, Belgium, Pathology Department, [3] GHDC, Charleroi, Belgium, Medical Oncology Department, [4] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Department of Medical Oncology, [5] GHDC, Charleroi, Belgium, Department of Medical oncology, [6] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Unit of Hepato-biliary and Pancreatic Surgery, Department of Digestive Surgery, [7] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Department of Abdominal Surgery and Transplantation, [8] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Department of Digestive Oncology, [9] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Support Statistique, [10] Université Paris Descartes, Paris, France, INSERM, Laboratory of Integrative Cancer Immunology, Sorbonne Université, [11] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Department of Digestive oncology.

Introduction: Surgical resection of colorectal liver metastases (CRLM) aims to maximize patient survival. However, recurrence rates remain high post-surgery. We previously reported the prognostic relevance of pathological response (PR) and histopathological growth pattern (HGP) of resected CRLM. Several studies have highlighted the existence of intratumor heterogeneity, which could also contribute to the mechanisms of anti- cancer drug resistance and patient's prognostic.
Aim: This study aims to explore tumor homogeneity for PR and HGP and understanding its potential prognostic implications.
Methods: Tumor homogeneity for PR and HGP was evaluated in 2 independent cohorts of patients. Cohort 1 was composed of 57 patients with resection of 159 CRLMs after chemotherapy and bevacizumab (prospective multicentric BEV-ONCO trial). Cohort 2 included 221 patients who underwent curative resection of 582 CRLMs with or without preoperative treatment at Cliniques universitaires Saint Luc and Grand Hôpital de Charleroi between 2005 and 2016. The pathological parameters of each CRLM were evaluated: PR according to tumor regression grade (TRG) classification (TRG 1 to 5) and HGP based on the morphology of the tumor–non tumor liver interface (desmoplastic, pushing, replacement or mixed if more than 1 pattern was observed in the same CRLM). High TRG (TRG 4–5) reflects non-PR and low TRG (TRG 1–2–3) meaning complete, major or minor PR. In patients with multiple CRLM, Max-TRG (higher TRG among all the CRLM) was used to define PR. Homogenous TRG and HGP was defined when all the CRLM of the patient had the same TRG or HGP pattern. HGP mixed pattern in one single CRLMs was considered heterogeneous by definition. Overall survival (OS for both cohorts), progression-free survival (PFS for cohort 1) and time to relapse (TTR for cohort 2) were estimated using the Kaplan–Meier method and compared by log-rank tests. Cox proportional hazard models were used for univariate analysis.
Results: Patients' and disease's characteristics were globally similar in both cohorts excepted for preoperative treatment. In cohort 1, Max TRG lower or equal than3 was significantly associated with favourable PFS (HR=0.41; 95CI: 0.202-0.835, p=0.014) but not OS (HR=0.34; 95CI: 0.105-1.114, p=0.075). HGP replacement and mixed was significantly associated with worse PFS (HR= 2.21; 95CI: 1.121-4.375, p= 0.022) but not OS (HR= 1.24; 95CI: 0.426-3.586, p=0.697). In cohort 2, Max TRG lower or equal then3 was only associated with favorable OS (HR=1.64, 95CI: 1.00-2.68, p=0.0471) while HGP replacement and mixed only associated with worse TTR (HR=1.84, 95CI: 1.33–2.56, p=0.0002). In cohort 1, homogeneous TRG s and HGP were significantly associated with a longer PFS (HR=0.21; 95CI: 0.101-0.435, p<0.001; HR=0.27; 95CI: 0.137-0.543, p<0.001) and better OS (HR=0.23; 95CI: 0.073-0.701, p=0.010; HR=0.32; 95CI: 0.107-0.932, p=0.037). Interestingly, same significant results were observed in cohort 2 for TTR (homogenous TRG: HR=0.60; 95CI:0.43-0.85, p=0.0036; Homogenous HGP: HR=0.68;95CI:0.49-0.94, p=0.0175) and OS (homogenous TRG: HR=0.51; 95CI: 0.33-0.80, p=0.0029; Homogenous HGP: HR=0.63; 95CI:0.41-0.97,p=0.0341). Homogeneous HGP reported a significant association with TRG homogeneous (p=0.012), a Max-TRG lower or equal than 3 (p=0.002), an absence of HGP replacement and mixed (p<0.001), a desmoplastic pattern (p=0.003), and the absence of sinusoidal obstruction syndrome (p=0.048) in cohort 1 (association currently investigated in cohort 2).
Conclusions: Homogeneity for PR and HGP observed on resected CRLMs is strongly associated with patient's survival and justifies further comprehensive research and validation studies.

- O04 -

CLINICAL IMPACT OF 99MTC-MAA SPECT/CT-BASED PERSONALIZED PREDICTIVE DOSIMETRY IN SELECTIVE INTERNAL RADIOTHERAPY: A RETROSPECTIVE, SINGLE-CENTER STUDY FOR UNRESECTABLE HCC PATIENTS. A.-M. BUCALAU (1), B. COLLETTE (2), I. TANCREDI (3), M. VOUCHE (4), M. PEZZULLO (3), R. MORENO-REYES (2), N. TROTTA (2), J. VAN LAETHEM (5), G. VERSET (5) / [1] Hopital Erasme, ULB, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, [2] CUB Hôpital Erasme, Belgium, Department of Nuclear Medicine, [3] CUB Hôpital Erasme, Belgium, Department of Radiology, [4] CUB Institut Jules Bordet, Brussels, Belgium, Department of Radiology, [5] CUB Hôpital Erasme, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology.

Introduction: Recent data indicates that personalized dosimetry-based selective internal radiotherapy (SIRT) may be associated with better outcome for unresectable hepatocellular carcinoma. Nevertheless, due to the negative results of several randomized studies, the future of selective internal radiation therapy (SIRT) in the management of hepatocellular carcinoma (HCC) is clouded. However, these different studies were performed without personalized dosimetry.
Aim: The aim of our study is to evaluate the contribution of personalized predictive dosimetry (performed with Simplicity90® software) in HCC patients treated with SIRT by comparing them to our historical cohort treated with Y90 whose activity to be injected was determined by standard, or so-called non-compartmental predictive dosimetry.
Methods: This is a retrospective, single-center study conducted between February 2016 and December 2020 that included patients with HCC not candidates for curative treatment who received SIRT (by Y90-loaded glass microspheres) after simulation based on either standard dosimetry (group A); or, as of December 2017, on customized dosimetry (group B). For Group B patients, the activity to be delivered was calculated using Simplicit90Y® software in order to obtain personalized dosimetry based on a multicompartmental approach. The primary objective was the evaluation in both groups of the response at 3 months, according to mRECIST, in terms of best overall response (per patient) and objective response (per nodule). For secondary objectives, we evaluated for both 2 groups: (1) progression-free survival (PFS) and overall survival (OS); (2) safety by collecting clinical and biological side effects, according to CTCAE V5. 0, at 24 hours, 1 and 3 months and radiological complications at 3 months; (3) for group A we studied the dose-response relationship at 3 months and compared the activity to be administered determined a posteriori using Simplicit90Y® and the activity actually administered determined by the non-compartmental approach using a target volume based on single-photon emission computed tomography (SPECT) of the distribution of Tc99m-labeled albumin macroaggregate (MAA) only (for patients treated prior to the use of Simplicit90Y® software).
Results: Between February 2016 and December 2020, 66 patients received 69 simulations leading to 40 treatments. A first difference observed was the higher number of patients not suitable for SIRT after simulation with the use of Simplicit90Y®, 24.1% for group A versus 56.8% for group B. The per patient analysis revealed a significant benefit of personalized predictive dosimetry in terms of better overall response at 3 months (80% vs. 33.3%, p= 0.007) and at 6 months (77.8% vs. 22.2%, p= 0.06). This trend was found in the analysis by nodule with a response rate according to mRECIST of 87.5% for personalized dosimetry versus 68.4% for standard dosimetry at 3 months, p= 0.24. The median follow-up time was equal for both groups, 21 months (range 3-55) in group A and 21 months (range 4-39) in group B. There was no treatment-related mortality at 1 month. Only one grade 3 biological toxicity (hyperbilirubinemia) was noted and persisted over time in the standard group. In terms of radiological complications, 5 asymptomatic peritumoral ischemic lesions were found in group B and 6 in group A. For group A, the comparison between the administered activity and the recommended activity recalculated a posteriori using Simplicit90Y® showed that the vast majority of patients who progressed received less activity than that recommended (83.33%) by the personalized approach or they presented an inadequate distribution of the administered activity, due to poor targeting that could have been anticipated by this same approach.
Conclusions: Our study confirms that the use of personalized dosimetry allows a better selection of HCC patients who can benefit from SIRT, and consequently, improves the effectiveness of this treatment.

- O05 -

DEVELOPMENT OF A NOVEL OFF-THE-SHELF CELL-BASED IMMUNOTHERAPY TO ERADICATE CD70-POSITIVE CANCER ASSOCIATED FIBROBLASTS IN METASTATIC COLORECTAL CANCER. A. Van Den Eynde (1), J. Van Audenaerde (1), J. De Waele (1), T. Flieswasser (1), H. Lau (1), J. Jacobs (2), M. Peeters (1), F. Lardon

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Introduction: Colorectal cancer (CRC) unfortunately retains its position as one of the most prevalent and lethal types of cancer worldwide. Moreover, occult clinical manifestations result in a substantial group of metastatic CRC patients with a grim 5-year survival due to ineffective treatment options. Increasing knowledge on the biological complex tumor microenvironment pinpoints cancer-associated fibroblasts (CAFs) as an important factor hampering effective treatment. Our lab identified a population of CAFs with strong expression of the immune checkpoint molecule CD70 harboring tumor-promoting properties. Targeting these CD70-positive CAFs might show great potential in (1) improving systemic therapy by permeabilizing the shield surrounding the tumor, (2) eradicating a permissive niche for tumor invasion and (3) alleviating immune suppression. In this regard, chimeric-antigen receptor (CAR)-immunotherapy is on the rise as highly promising cell-based immunotherapy. Compared to the extensively studied CAR-T cells, CAR-natural killer (NK) cells serve as an attractive, allogeneic, off-the-shelf alternative eliminating the need for personalized and patient-specific products, thereby enabling fast and sufficient adoptive cell transfer.
Aim: We aim to generate off-the-shelf CAR-NK cells capable of eradicating CD70-positive CAFs.
Methods: The human NK-92 cell line was used as inexhaustible source for developing CD70-targeting CAR-NK cells. Generation was accomplished by electroporating our in-house created and optimized CD70 CAR mRNA construct into the NK-92 cell line. Validation of the CAR expression on the cell surface of the NK-92 cell line was determined via flow cytometry. Proof-of-concept in vitro killing capacity of the CD70-directed CAR-NKs was assessed by a coculture experiment with the highly CD70-positive, NK-resistant, Burkitt lymphoma Raji cell line. After 4 hours, cell death of the target cells was measured with flow cytometry by staining for the viability intercalating fluorescent dye 7-AAD and the apoptotic cell death marker Annexin V. To differentiate effector and target cells, the latter were transiently labeled with PKH67, a green fluorescent dye.
Results: Electroporation of CAR mRNA into the NK-92 cell line could successfully generate CD70-targeting CAR-NK cells. Nearly all electroporated NK-92 cells (>90%) showed high CAR expression over 72 hours with the highest expression seen after 24 hours. Furthermore, the developed CAR-NK cells were also able to eradicate more than 80% of the CD70-positive Raji cell line in 4 hours compared to approximately 20% in the control condition. At this very moment we are performing experiments to confirm our proof-of-principle in eradicating CD70-positive CAFs in CRC.
Conclusions: Our data demonstrate the successful generation of CD70-directed CAR-NK cells with strong CAR expression and robust killing capacity. These results lay the foundation for further investigating CD70-directed CAR-NK cells in mCRC patients.

- O06 -

INTRODUCTION OF PERCUTANEOUS STEREOTACTIC MICROWAVE ABLATION (SMWA) AS ALTERNATIVE FOR LIVER RESECTION IN MALIGNANT LIVER TUMORS DURING PANDEMIC HOSPITAL RESTRICTIONS.

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Introduction: Liver surgery for resectable malignant liver tumors, such as colorectal liver metastasis (CRLM), non-colorectal liver metastasis (NCRLM) and hepatocellular carcinoma (HCC), is still considered the standard local therapy. Resection, radiofrequency ablation (RFA) or microwave ablation (MWA) of CRLM or HCC with a diameter <3 cm have similar overall survival. Percutaneous RFA or MWA under CT guidance is considered less invasive than by surgical approach. However, percutaneous RFA or MWA by “free-hand” puncture is considered less accurate, resulting in higher incomplete ablation and local recurrence rates. Moreover, “free-hand” puncture is mainly performed in axial planes, resulting in difficult approach of lesions in the upper liver segments 4A, 7, 8, due to their subphrenic position. Tumors in segment 1 are difficult to reach by “free-hand” due to close relationship with main vascular structures. Stereotactic navigation technology, allows safe and easy puncture in these difficult localizations, resulting in high local response rates. Finally, the Covid19 pandemic resulted in strict capacity limitations in OR, hospitalization and ICU. Liver surgery requires optimal OR facilities and often postoperative ICU care.
Aim: To avoid unacceptable delay in oncologic liver resections during pandemic hospital restrictions, percutaneous stereotactic microwave ablation (SMWA) was introduced in our hospital. Oncologic equivalence, postoperative outcome and impact on hospital resources of this new therapeutic strategy are analyzed.
Methods: From March 2020 till November 2021, all resectable CRLM, NCRLM and HCC with a diameter ≤ 3 cm were treated by SMWA under CT guidance with stereotactic technology (Cascination®). CRLM, NCRLM and HCC with a diameter between 3cm and 5cm were also treated by SMWA, if resection was considered less safe according to surgical-technical, patient-related or pandemic restriction reasons. Local treatment efficacy was assessed by MRI after 2 month and stratified into complete local response (CR) and incomplete or partial local response (PR). Patients with progressive disease outside the areas treated by SMWA were excluded for analysis. Postoperative morbidity (Clavien-Dindo), mortality, ICU stay, hospital stay and OR time were recorded. These latter 2 data were compared with a historical cohort of liver resections for similar indication. Tumor type, tumor size and tumor localization in difficult liver segments 1,4a,7,8, subcapsular, or adjacent to main portal or hepatic veins were analyzed if predictive for PR.
Results: 105 patients were treated by SMWA. In 83 patients MRI at 2 months was available. 5 patients had progressive disease outside the areas treated by SMWA. 78 patients with 140 liver tumors were included in this analysis. Median age was 67y (33-92y). In 74/78 (95%), no complications (Clavien 0 or 1) occurred. There was no postoperative mortality, no ICU stay was required. Hospital stay was 1 overnight stay in 68/78 (87%), only 1/78 stayed longer than 3 nights. Hospital stay was shortened by 3.7 days and OR time by 3.6h per patient compared to the resection cohort. After 1 session of SMWA, CR was achieved in 70/78 (89.7%); after redo SMWA for PR, CR was achieved in 77/78 (98.7%). PR was seen in 8/140 tumors (5.7%). Tumor type and tumor size were not predictive for PR (CRLM: 6/77, 7.8%; NCRLM: 1/26, 3.7%; HCC: 1/35, 2.8%; size <3cm: 7/124, 5.6%; size > 3cm: 1/16, 6.3%). Tumor localization was not predictive for PR (in segments 1,4a,7,8: 4/75, 5.3%; subcapsular: 4/43, 9.3%; adjacent to main portal/hepatic veins: 2/25, 8%).
Conclusions: Stereotactic MWA of liver tumors <5cm can be performed as an alternative for liver resection. It allows very accurate needle positioning in all liver segments, with equivalent local response rate in tumors localized in the upper or “difficult” liver segments or close to major vascular structures. Moreover, a second SMWA can be performed in case of incomplete ablation, resulting in 99% of local tumor control. SMWA is very well tolerated as a minimal invasive procedure, resulting in low postoperative morbidity and hospital stay. It has the potential to avoid Covid19-related postoperative complications compared to liver resection surgery. SMWA has a lower impact on hospital resources and can be continued as an equivalent alternative for liver resection surgery during temporarily reduced hospital capacities.

- O07 -

DEEP EPIGASTRIC LYMPH NODE (DELN) BASIN AS A POSSIBLE SYSTEMIC METASTATIC PATHWAY OF PERITONEAL METASTASES: A RETROSPECTIVE ANALYSIS ON PATIENTS WITH RECURRENT PERITONEAL CARCINOMATOSIS.

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Introduction: Metastatic colorectal cancer (CRC) constitutes one of the leading causes of cancer-related deaths worldwide. 20% of patients with CRC will develop peritoneal metastasis (PM) during the course of their disease. Cytoreductive surgery (CRS) +/- HIPEC remains the standard treatment for PMCRC in a selected number of patients. However, most of the patients operated for PMCRC, ultimately develop distant recurrences, suggesting a systemic dissemination of the disease. Whether this malignant dissemination comes from the primary cancer and/or from the PM itself, the need for a channelling route brings the lymphatic system into the spotlight, as a fundamental system in any cancer metastatic process. Elias et al were the first to report the role of cardio-phrenic angle lymph nodes (CPALN), as a primary drainage basin of the peritoneum through the diaphragm, in patients with PC of colorectal origin. However, we have recently demonstrated the existence of a lymphatic basin, the Deep Epigastric Lymph Nodes (DELN) at the level of the inferior epigastric artery, harboring metastatic tumoral cells in patients presenting with PM of colorectal and ovarian origins. This DELN can represent a possible dissemination pathway from the peritoneum to the extraperitoneal compartments in patients with PMCRC.
Aim: The objective of this study was to evaluate the DELN role and radiological involvement, in patients with recurrent CRC (after CRS ± HIPEC for PM) and to assess the implication of the DELN in the global recurrence pattern of these patients.
Methods: This is a retrospective study including patients treated for peritoneal metastasis from colorectal origin with curative intent, from 2012 until 2018, at our institution, and who presented with any type of disease recurrence. All CT scans were reviewed to identify the recurrent metastatic sites, and to locate the enlarged lymph nodes: at the DELN basin, the cardio-phrenic angle (CPA) level, the posterior retroperitoneal compartment, and the distant lymphatic sites.
Results: Amongst the 50 patients included, 29 patients (58%) had radiological lymph nodes involvement, versus 21 patients (42%) with no radiologically involved lymph nodes. The deep epigastric basin was involved in 8% of the patients. This group of patients had a higher PCI median (18) than all the other groups (6.5 in distant LNs; 4 in Retroperitoneal LNs, and 4.5 in CPALNs). Furthermore, patients in this group had the highest incidence (100%) of peritoneal involvement upon recurrence, when compared to the other groups.
Conclusions: Our study confirms the potential role of the anterior abdominal lymphatic pathway, previously overlooked, in the systemic dissemination process of colorectal PM. We hereby shed into light a previously unrecognized lymphatic

pathway, as an intermediate checkpoint, a relay, between the peritoneum, as an intra-abdominal organ, and the extra-abdominal compartment.

- O08 -

FOLLOWING THERAPY RESPONSE THROUGH LIQUID BIOPSIES IN METASTATIC COLORECTAL CANCER PATIENTS: THE LEAD-IN FOLICOLOR TRIAL. K. Janssens (1), K. Op De Beeck (2), S. Raats (3), S. Wouters (3), G. Van Camp (1), M. Peeters (4) / [1] University of Antwerp/Antwerp University Hospital, Edegem, Belgium, Center of Medical Genetics (CMG), [2] University of Antwerp/Antwerp University Hospital, Edegem, Belgium, Center of Medical Genetics (CMG)/ Center for Oncological Research (CORE), [3] Antwerp University Hospital, Edegem, Belgium, Multidisciplinary Oncological Center Antwerp (MOCA), [4] University of Antwerp/Antwerp University Hospital, Edegem, Belgium, Oncology Department/Center for Oncological Research (CORE).

Introduction: It is widely accepted that liquid biopsies and the analysis of circulating tumour DNA (ctDNA) hold great potential for the follow-up of metastatic colorectal cancer patients (mCRC). However, prospective trials on the implementation of liquid biopsies in practice and whether patients benefit from this approach are still lacking. NPY methylation is a known tumour specific biomarker in colorectal cancer patients. It is associated with tumour burden and can be used as a follow-up biomarker of mCRC patients according to several publications. However, previous studies (with liquid biopsies collected at only a few timepoints) did not collect enough data to determine the optimal methylation cut-off value of this marker to predict progressive disease on CT imaging.
Aim: Therefore, we designed a study to determine the optimal cut-off value of NPY methylation to detect progressive disease in mCRC patients. Furthermore, we will compare the use of ctDNA and CEA to predict progression.
Methods: In this prospective, multicentre, interventional study, patients with RAS and BRAF wild-type mCRC, starting first-line treatment with FOLFOX or FOLFIRI combined with panitumumab received follow-up with biweekly liquid biopsies and CT imaging every 8 weeks. Patients were followed for 9 months or until curative metastasectomy. Three Streck tubes were collected at each timepoint and centrifuged using a two-step high-speed centrifugation protocol (10 min 1,900g and 10 min 16,000g). CfDNA extraction was done using the QIAsymphony DSP Circulating DNA Kit (Qiagen) and quantified with the Qubit 2.0 fluorometer with the dsDNA high sensitivity assay (Thermo Fisher Scientific). CfDNA samples were bisulphite converted using the EZ DNA Methylation kit (Zymo Research) and subsequently analysed for NPY methylation using the QX200 digital droplet PCR system (Bio-Rad). Data from ddPCR were processed with the QuantaSoft v1.0 software (Bio-Rad) and statistical analysis was performed using R version 3.6.
Results: Twenty patients were included from 7 centres in Belgium between 28/12/2020 and 28/07/2021. However, five patients were ultimately excluded due to a pathogenic KRAS mutation (2), a BRAF V600E mutation (2) or no treatment with panitumumab (1). The final population of 15 patients consisted of 11 males and 4 females with a median age of 73 years. At baseline 14/15 (93%) patients had detectable NPY methylation in the liquid biopsy (median NPY methylation ratio 22.22%, range 0.00-87.81%). The median NPY methylation ratio decreased to 0.21% (range 0.00-4.35%) after 2 cycles of therapy and to 0.01% (range 0.00-1.77%) after 4 cycles of therapy (both significant decrease, $p = 0.001$). A decrease in NPY methylation ratio after 2 cycles of therapy corresponded to response (partial response or stable disease according to RECIST guidelines) on first CT imaging (after 4 cycles of therapy). At the moment of this first analysis, the median follow-up was 227 days and four patients already reached end of study (2 underwent curative metastasectomy and 2 reached 9 months of follow-up). One patient developed progressive disease (detection of new lesion) during a therapy break of 49 days after 12 cycles of therapy (FOLFOX + panitumumab). At that time, the NPY methylation ratio increased from undetectable to 1.89% and there was no increase in CEA (decreased from 6.10 to 4.87 µg/L). Further follow-up and liquid biopsy collection are ongoing and additional results will be presented at the conference.
Conclusions: The results of the first analysis of the lead-in FOLICOLOR trial confirm that a decrease in NPY methylation ratio after two cycles of therapy predicts response on first evaluation. NPY methylation is also a promising marker for early detection of progressive disease in mCRC patients. However, until now, only one patient has shown progressive disease in this study population so additional data is required to draw a conclusion.

- O09 -

USING CT SCANS TO MEASURE SARCOPENIA IN DIGESTIVE CANCER PATIENTS. A. Van Oosterwyck (1), K. Plovie (1), M. Cool (1), G. Deboever (1), G. Lambrecht (1) / [1] AZ Damiaan, Oostende, Belgium, Gastroenterology and Digestive Oncology.

Introduction: Sarcopenia, the progressive and generalised loss of skeletal muscle mass and function, is commonly seen in patients with chronic disease and in the elderly. One of the big causes of sarcopenia is cancer, especially digestive cancers. More and more data suggest that sarcopenia in cancer patients leads to poor outcome with regard to overall survival, chemotherapy toxicity and postoperative complications. Therefore, we want to screen digestive cancer patients effectively to start timely nutritional interventions. One of the tools we have is bioelectrical impedance analysis (BIA). However, this does not always produce an accurate prediction, given the many confounding factors such as hydration status. It can also be time consuming, and good equipment is an investment. Determination of skeletal muscle index by analysis of cross-sectional CT scan images is a known technique to accurately define sarcopenia, but is not the golden standard because of cost and radiation. However, in cancer patients, we have access to a staging CT scan at the point of diagnosis, which gives us an excellent opportunity to also screen for sarcopenia and optimize nutritional status before and during treatment.
Aim: The aim of this study was to prove the convenience and value of cross-sectional skeletal muscle index determination as a measurement of sarcopenia in digestive cancer patients, compare the results with BIA (when executed) and note the effect on chemotherapy toxicity and mortality. This was a retrospective observational study with a very heterogeneous population.
Methods: We used the staging CT scan of digestive cancer patients at diagnosis to determine whether they were sarcopenic, and checked whether this was correspondent with BIA measurements when available. We also noted if there was more significant chemotherapy toxicity that required dose adjustment, deferral or hospital admission due to neutropenic fever in the sarcopenic group. We only checked for toxicity in the first course of treatment since the adverse effects of treatment itself can cause sarcopenia and toxicity. Lastly, we also evaluated mortality in both groups. The software we used to achieve this was the medical image analysis software SliceOmatic. We measured the combined cross-sectional surface of all muscles (i.e. external and internal oblique, transverse, psoas and paravertebral muscles) on a transverse CT image at the level of the third lumbar vertebra (L3). This number was then divided by the square of the height. This number is the skeletal muscle index (SMI). There is no consensus yet about the cutoff values, the ones we used in this study were <39 cm^2/m^2 for women and <55 cm^2/m^2 for men, as developed for the oncological population by Mourtzakis et al.
Results: Overall, we evaluated 63 patients with different digestive tumours at all stages: 17 esophageal, 14 pancreatic, 13 stomach, 8 colon and 5 rectal tumours, 4 cholangiocarcinomata and 2 neuroendocrine tumours. Of these 63 patients, 43 (68%) were sarcopenic. In 28 patients (44%) we also had access to BIA measurements. These measurements were concordant in only 13 (46%) patients, with only 33% of concordant analyses being 'true positive', meaning they detected sarcopenia when there was also sarcopenia according to SMI. 21 of 36 (58%) sarcopenic patients experienced dose-limiting chemotherapy toxicity in the first cycle of chemotherapy, if chemotherapy was started, whereas 7 of 19 (37%) patients without sarcopenia needed dose reductions or deferrals. Finally, mortality was higher in the sarcopenia group compared to the non sarcopenic patients, 44% and 26% respectively.
Conclusions: In conclusion we think that L3 SMI is a very feasible and convenient method of determining sarcopenia in high risk digestive cancer patients. A lot of patients are missed with the more conventional BIA method. Given that in these patients, we always have access to staging CT-scans, it is easy to perform an extra analysis in our global nutrititonal assessment and adequately start treating pre-existing sarcopenia before cancer directed therapy starts and muscle mass may further decline. We also noted a higher rate of chemotherapy toxicity and higher mortality, though it is of course hard to draw conclusions as this was a very heterogeneous and small population, and sarcopenia might also be a direct consequence of more progressive disease. Future prospective studies with regard to dose reduction based on sarcopenia, as well as nutritional intervention would be helpful.

- O10 -

OCCURRENCE AND TREATMENT OF BRAIN METASTASES IN PATIENTS WITH DIGESTIVE CANCERS – A SINGLE CENTRE RETROSPECTIVE REVIEW. I. Ould-Nana (1), D. Castanares Zapatero (2), I. Borbath (1), A. De Cuyper (3), M. Van Den Eynde (4) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Gastroenterology, [2] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Intensive Care Unit, [3] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Medical Oncology, [4] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Gastroenterology.

Introduction: Metastatic cancers expose patients to multiple complications, the most redoubtable of them are brain metastases (BM). However, they are rare in digestive cancers, occurring in 1 to 4%, thus not justifying systematic cerebral imaging for asymptomatic patients.
Aim: The aims of this retrospective descriptive study were to characterize the disease history of patients with BM from digestive cancers, to explore possible clinico-pathological prognostic factors and the impact of treatments.
Methods: All digestive cancers patients who developed brain metastases and treated at the Cliniques universitaires Saint-Luc between 01/2001 and 12/2020 were analysed. Inclusion criteria included confirmed histologically primary digestive cancer (including colorectal (CRC), oeso-gastric (OGC) and hepato-biliary-pancreatic cancers (HBPC)) with BM documented by imagery. Patients with synchronous non-digestive cancers were excluded. Available clinico-pathological informations, BM characteristics, systemic and local BM treatments as well as clinical and survival follow-up were extracted from the electronic medical records. Statistical analysis was performed using the SPSS v28. Univariate analysis was performed using Kaplan-Meier survival curves for patient metastatic overall survival (OS) since the metastases diagnosis and patient brain OS / progression-free survival (PFS) since the BM diagnosis. A p-value of 0.05 or less was used as a criterion for significance. Approval for this retrospective research was obtained from the ethics committee of the Cliniques universitaires Saint-Luc.

Results: Out of 1722 patients, 73 presented brain metastases (4.2%). Included patients (median age: 60 y-old) were more often male (n=45/73; 61.6%) with colorectal cancer (n=54/73; 74%), extra-cerebral metastases (n=60/73; 82.2%), history of primary tumor surgery (n=59/14; 80.8%) and at least 1 systemic treatment before BM diagnosis (n=64/73; 87.6%). Occurrence of BM was limited to 1 lesion in 49.3% (n=36/73), exclusive in 17.8% (n=13/73), symptomatic in 87.7% (n=64/73), with oedema in 84.9% (62/73). BM local treatments included surgery (n=28/73; 38.4%), stereotactic radiotherapy (SRT) (n=14/73; 19.2%) and panencephalic radiotherapy (PERT) (n=34/73; 46.6%). Multiple sequential local BM treatments were applied in 17,8% (n=13/73) of patients, while 24.7% (n=18/73) did not receive local BM treatment. Median time from metastases diagnosis to BM occurrence was 30.4 months for CRC and <1 month for OGC and HBPC. Median metastatic OS was 30,9 months (39.6, 17.8 and 1.5 months for respectively CRC, OGC and HBPC, p= 0.002). The median brain OS was 4,7 months (4.8, 5.6 and 1.2 months for respectively CRC, OGC and HBPC, p= 0.003). The median brain PFS was 2,6 months (3.2, 4.5 and 0.5 months for respectively CRC, OGC and HBPC, p= 0,0001). CRC or OGC, primary tumor surgery, ≤4 brain metastases, local ablative treatment (surgery or SRT) were significantly associated with favorable brain OS and PFS in univariate analysis.
Conclusions: Brain metastases are rare, occur late in the disease history of patients with CRC and remain of poor prognosis. Surgery and SRT seem to be associated with some local efficacy and limited survival benefit.

- O11 -

A SYSTEMATIC REVIEW TO PREDICT THE OUTCOME OF PHASE III CLINICAL TRIALS IN GI ONCOLOGY. G. Bregni (1), R. Saúde Conde (1), G. Rasschaert (1), T. Akin Telli (1), A. Hendlisz (1), F. Sclafani (1) / [1] Institut Jules Bordet, Brussels, Belgium, Medical Oncology.

Introduction: Despite major efforts to develop new and effective anticancer therapeutics, rapid advances in oncology care are constrained by the high failure rate of late phase clinical trials, only a small proportion of initially promising investigational compounds being ultimately granted regulatory approval. This is especially true for gastrointestinal (GI) cancers, for which drug discovery has historically lagged behind other tumour types. Identifying pitfalls of the drug development process, and establishing objective criteria for the go/no-go decision making could increase the probability of success of late phase clinical trials.
Aim: To assess the association between the quality of existing evidence prior to the conduct of phase III (P3) trials and the outcome of the same, and to identify objective parameters from earlier phase studies that could predict success/ failure of subsequent P3 trials.
Methods: This was a systematic review. Two investigators independently searched EMBASE, PubMed, and proceedings from major international meetings (ESMO, WCGIC, ASCO and ASCO GI Cancers Symposium) for all reported randomised P3 trials in GI cancers (including gastro-oesophageal (GEC), hepatocarcinoma (HCC), biliary tract (BTC), pancreatic (PC), small bowel (SBC), colo-rectal (CRC), anal (AC), gastrointestinal stromal tumour (GIST), and neuroendocrine cancers (NET) between January 2000 and June 2020. Potential relevance of the retrieved studies was assessed by reading titles and abstracts. Eligibility was restricted to P3 trials for advanced disease, with a superiority design, and using standard of care treatment as control. Trials were excluded if testing previously approved drugs, comparing different schedules of the same compound, investigating non pharmacologic interventions, supportive care agents, or prevention strategies, or not reporting complete study results in relation to the primary endpoint. If multiple reports from the same trial were available, the latest paper/abstract reporting complete efficacy results was used for data extraction. Existing evidence supporting the conduct of each P3 trial was retrieved from the main study report, and data from the corresponding earlier phase trials were extracted from the main study publication. Trials were considered positive if they met the pre-defined primary end point.
Results: 185 P3 trials were included (GEC=53, CRC=47, PC=37, HCC=30, NET=8, BTC=5, GIST=5) recruiting a total of 74,013 patients. Of these, 67 (36.2%) were positive, 117 (63.2%) negative, 1 (0.5%) unknown (no formal hypothesis reported). Positivity rates were 37.7% for GEC, 48.9% for CRC, 18.9% for PC, 16.7% for HCC, 75% for NET, and 60% for BTC and GIST. Information about quality of prior evidence was available for 184 P3 trials. Of these, 67 (36.4%) had no prior phase II (P2) study: 19 GEC (36.5%), 23 CRC (48.9%), 13 PC (35.1%), 5 HCC (16.7%), 0 NEC (0%), 2 BTC (40%), 3 GIST (60%). The probability of success was 35.9% for P3 trials preceded by P2 studies and 35.8% for those lacking prior P2 studies (p=0.989). In 32 cases (17.4%), P3 trials followed randomised P2 studies, which were positive in 15 (46.9%), negative in 16 (50%), and unknown (formal hypothesis lacking) in 1 case (3.1%). P3 trials with pre-existing positive randomised P2 evidence had higher chances to meet their primary endpoint than those designed after negative randomised P2 studies (40% versus 18.8%).
Conclusions: To our knowledge, this is the largest study ever conducted to evaluate factors that can predict the outcome of P3 trials in GI oncology. Our results show that only a minority of these meet their primary endpoint, this confirming the urgent need to improve the drug development process in this disease setting. In approximately one third of cases, P3 trials are informed by preliminary data from phase I studies. While quality of the pre-existing evidence does not appear to influence the outcome of subsequent P3 trials, the probability of success increases if the P3 study design is supported by the positive results of a prior randomised P2 study. Additional data about the predictive value of a number of parameters from studies preceding P3 trials will be presented at the Meeting.

- O12 –

INITIAL ESTABLISHMENT OF PATIENT-DERIVED ORGANOIDS AS A NOVEL MODEL FOR NEUROENDOCRINE NEOPLASMS. O. Islam (1), V. Timon (1), M. Lecompte (2), C. Deben (2), G. Roeyen (3), N. Komen (4), S. Peeters (2), F. Rodrigues Fortes (2), M. Peeters (1), W. Lybaert (1), H. Prenen (1), F. Lardon (2), A. Driessen (5), M. Huizing (1) / [1] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Oncology, [2] University of Antwerp, Antwerp, Belgium, CORE, [3] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Hepatobilliairy Surgergy, [4] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Abdominal Surgery, [5] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Pathology.

Introduction: Gastroenteropancreatic neuroendocrine neoplasms (GEP-NEN) are a group of heterogeneous neoplasms that arise from neuro-endocrine cells, which is subdivided in small intestinal NENs (siNENs), the most common tumour in the small intestine with an incidence of 1.05 per 100,000 person years and pancreatic NENs (pNENs) representing about 1-2% of all pancreatic neoplasms, with an incidence of about 0.48 per 100,000 person years1,2,3. NEN's are classified based on their tumour morphology and proliferation rate. Well differentiated NEN's have a relative long overall survival. NEN's in general are poorly understood and because of the limited treatment options, more aggressive forms such as gastroenteropancreatic neuroendocrine carcinoma (GEP-NEC) can have a poor prognosis. In order to better understand neuroendocrine neoplasms, several associations have been instituted, such as "NETwerk", which is a collaboration between eight Flemish hospitals. NETwerk's purpose is to improve diagnosis and treatment of NEN's by introducing a shared database and permitting clinicians to access data from all participating hospitals. Patients included in the NETwerk database are discussed regularly at multidisciplinary oncological consult, ensuring that patients get an optimized and individualized treatment plan4, but there is a lack of proper preclinical models and only a few representative preclinical models are available. So there is a necessity to create proper models with the right patient characteristics to characterize mechanisms of drug resistance and to test novel therapies. That is why we would like to create a biobank with patient tissue, blood and patient derived 3D organoids which would represent the original NET tumour to use as model for translational research.
Aim: Our first aim is to successfully create NET organoids, both siNET and pNETs, which then can be used in translational research. In the initial phase we would like to culture 3D organoids from fresh tissue samples using recent knowledge on culturing pancreatic duct adenocarcinomas (PDAC's) and combined with literature research on using the right methods, culture environment and culture medium within the CORE lab (Centrum for Oncological Research of the University of Antwerp). NEN organoids will be checked for similar morphological, genetic and phenotypical characteristics as the tumour in vivo. After successful establishments, resistance mechanisms and new treatment options will be evaluated using drug screenings using the real-time OrBITS drug screening platform.
Methods: After obtaining an informed consent, fresh tumour tissue is collected during surgery and transported in DMEM Advanced (DMEM-F12) medium. We then process the tissue, one of the first steps is digesting the tissue by adding collagenase and incubating this for about one hour at 37 degrees Celsius. Before and after this step it is important to work on low temperatures or on ice to avoid apoptosis during the whole process. After further steps and centrifugation, we become a cell pellet which is then mixed with the matrix (Cultrex BMEs), a soluble form of basement membrane, which provides a natural extracellular matrix hydrogel. Our gel suspension is plated in well-plates, incubated for 30 minutes at 37 degrees Celsius and ultimately DMEM advanced together with several supplements and antibiotics is added as culture medium. The exact compounds of these supplements is still in an experimental phase and needs more fine-tuning.
Results: In this initial phase, we collected 3 fresh surgical patient samples of pancreatic NETs. These were processed in our lab, in the same way as PDAC's are processed as described above to obtain organoids. In our first sample we saw the first organoids after 10 days, while culture of the other samples is ongoing (<10 days). After the initial growth phase, we will check if the organoids histomorphologically resembles the original tumour. Further development and optimization is still ongoing and we expect to be able to present the further results during the meeting.
Conclusions: Organoids are good models which usually resemble the characteristics of the original tumour in vivo. In NET there is an important unmet need of these models. Once our organoids are obtained successfully, we will have great preclinical models for further testing, which can lead to strategies to go to a more personalized treatment strategy. So far, we have started with 3 patient samples, where the first sample started growing organoids.

- O13 –

IDENTIFICATION AND QUANTIFICATION OF THE MICROBIOME IN COLORECTAL CANCER METASTASES. P. Stevens (1), V. Llorens-Rico (2), P. Baldin (3), L. Craciun (4), S. Gofflot (5), F. George (6), J. Sadones (7), M. Buys (8), F. Sandras (9), J. Raes (2), M. Van Den Eynde (1) / [1] UCL Saint Luc, Brussels, Belgium, Medical Oncology, [2] KUL - University of Leuven, Leuven, Belgium, Laboratory of Molecular Bacteriology, Department of Microbiology and Immunology, Rega Institute, [3] UCL Saint Luc, Brussels, Belgium, Anatomical pathology department, [4] Institut Jules Bordet, Brussels, Belgium, Biobank department, [5] CHU of Liège, Belgium, Biobank department, [6] CHU UCL Namur, Yvoir, Belgium, Biobank department, [7] UZ Brussel, Jette, Belgium, Biobank department, [8] UZA,

Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Biobank department, [9] Erasme Hospital, Brussels, Belgium, Biobank department.

Introduction: Despite early evidence from metagenomics studies showing a role of the gut microbiome in the development of colorectal cancer (CRC), its part in promoting or aiding metastasis to distant organs remains poorly understood. Recent research has identified the existence of bacterial genomes and viable bacteria in human tumor tissue of different origins, as well as cancer-specific cell-free bacterial nucleic acids in the blood of patients. Interestingly, specific bacterial strains from primary CRC have been identified in patient-matched liver metastases. Few mechanistic hypotheses have been proposed of how bacterial translocation to distant sites occurs, or whether the tumor-resident microbiome can influence the behavior of metastasis and the local immune response.
Aim: We aim to identify and quantify bacterial taxa in primary colorectal tumors (PT) and associated metastases (CRCM), each with normal adjacent tissue (NAT) as control. We plan to enlighten to which extent the microbiome from the PT is transferred to CRCM and how it could be specific to tumor type and/or singular to patient.
Methods: We collected 389 frozen samples and clinical data from 99 patients from several tumor biobanks in Belgium, composed by: 106 PT with 83 NAT, 134 CRCM with 66 NAT. CRCM included locations from liver (N = 98), lung (n=18), peritoneum (n=9) and brain (n=7). In addition, we included a cohort of primary liver cancers (hepatocellular carcinoma (HCC, n=28) with HCC NAT (n=26) and cholangiocarcinoma (CGC, n=6) with CGC NAT (N = 3) as comparative cohort from 27 patients. Total DNA and RNA from all samples was extracted and the V4 region of the bacterial 16S rRNA gene was sequenced. The computational DADA2 pipeline was used to process the sequencing data and determine the abundance of amplicon sequence variants (or "ASVs", that is unique amplicon bacterial sequences that can be assigned to specific bacterial taxa). We used Rstudio software to analyze our data, including different packages (Phyloseq, MicroViz, Vegan, ZCompositions, CoDaSeq). Since the microbial biomass was expected to be lower into tissue, we strictly applied sterile conditions from sample collection to sequencing, with negative and positive controls along the process to minimize contamination and misinterpretation of the results. Potential contaminants were removed bioinformatically by applying a series of filters.
Results: We observed the presence of bacterial taxa in all collected tissues types. We identified three main clusters based on the sample type ((i)PT-NAT;(ii)CRCM-NAT;(iii)HCC-CGC-NAT) with significant differences in their microbiome composition. Preliminary results suggest that bacterial abundance and diversity is much richer in colonic samples (PT and associated NAT) than in all other sample types. Although there was a lower bacterial biomass in CRCM, the microbiome composition seems to be partially overlapping that of matched-patient PT and consisting with previously reported prevalent taxa in CRC. This similarity appears to be higher in intra-patient than inter-patient, cautiously suggesting a potential bacterial transfer from PT to CRCM in a same patient. Moreover, this transfer appears to be a probabilistic event, more likely for more abundant bacteria in PT. The bacterial composition of liver CRCM seems to be different from HCC-CGC samples, the latter having the lowest bacterial biomass, suggesting a "per-tumor type" rather than "per-organ" bacterial signature. As we deal with well-known low bacterial biomass in CRCM and HCC-CGC samples, bacterial contamination could have an impact on results and even though we have implemented stringent quality controls, we must validate our analyses with additional samples and comparative cohorts.
Conclusions: Bacterial taxa with different abundance and diversity were identified in CRC and metastases. Our first results could suggest potential bacterial transfer from PT to the CRCM. However, due to low bacterial biomass in non-colonic tissue, contamination is a major challenge for the result's interpretation. To address this problem, we have implemented a strategy to minimize and remove contaminants in our experiments and analyses, and our results will need to be validated on additional cohorts.

- O14 -

THERAPEUTIC YIELD OF COMPREHENSIVE MOLECULAR PROFILING IN CHOLANGIOCARCINOMA: A RETROSPECTIVE SINGLE CENTER STUDY.

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Introduction: Cholangiocarcinomas (CCAs) are rare and highly heterogeneous biliary malignant tumors that can arise at any site of the biliary tree. Each subtype (intrahepatic (iCCA), perihilar (pCCA) or distal (dCCA)) has a distinct epidemiology, biology, prognosis and strategy for clinical management. For patients with locally advanced or metastatic disease, the available systemic therapies are of limited effectiveness. In recent years, the introduction of next-generation sequencing (NGS) technologies opened new horizons for a better understanding of the genetic pathophysiology of CCA and consequently, for the identification of molecular alterations for targeted treatments.
Aim: The aim of this study was to identify the proportion of targetable alterations found in cholangiocarcinoma and to study the effect of targeted treatment on disease control.
Methods: We retrospectively collected the results of comprehensive genomic testing obtained in patients with locally advanced or metastatic cholangiocarcinoma in a single center between 1/12/2018 and 16/9/2021. Genetic profiling of the tumor was either done by in-house testing (SeqCap NGS, microsatellite instability (MSI) immune histochemistry (IHC), HER2 IHC and in-situ hybridization) or by FoundationOne CDx/FoundationOne Liquid CDx. Genomic findings were classified using the ESMO Scale for Clinical Actionability of molecular Targets (ESCAT).
Results: 125 patients were included with a median age at diagnosis of 65 years. Male/female proportion was 64/61 (51,2%/48,8%). Four patients had underlying primary sclerosing cholangitis (PSC). In-house testing was performed in 41 patients, FoundationOne CDx in 57 and FoundationOne Liquid CDx in 21 patients. 5 samples failed quality control. All subtypes of biliary tumors were included: 6 gallbladder cancers (4,8%), 1 mixed hepatocellular carcinoma/cholangiocarcinoma (0,8%), 65 iCCAs (51,2%), 32 pCCAs (26,4%), 19 dCCAs (15,2%), 1 ampullar carcinoma (0,8%) and 1 carcinoma of unknown primary with histologic features of CCA (0,8%). Class 1 alterations, defined as druggable in clinical routine, were found in 22,7% of patients and consisted of MSI-H (6,7%), FGFR2 fusions (9,1%) and IDH1 mutations (10,1%). NTRK fusions were not detected. 30 % of patients had a class 2 alteration (druggability under investigation) including MSS/TMB-high (2,3%), mutations in BRCA1 (2,0%), BRCA2 (3,0%), CHEK2 (3,0%), PALB2 (1,0%), ATM (4,0%), AKT1 (1,0%) or PIK3CA (8,1%), ROS rearrangement (2,0%), BRAF V600E mutations (2,0%), MET amplification (1,3%) and HER2 amplification (7,0%). 28,0 % and 20,0 % of patients with a class 1 and class 2 alteration respectively were treated with targeted treatment. With a median follow-up of 5,4 months, the median PFS on this targeted treatment was not yet reached.
Conclusions: In this large single center cohort, comprehensive molecular characterization led to the identification of targetable and potentially targetable alterations in a significant proportion of patients with locally advanced or metastatic CCA. Given the emergence of new targeted drugs and the limited effectiveness of standard chemotherapy, molecular analysis should be considered in all patients fit enough for systemic treatment.

BELGIAN PANCREATIC CLUB (BPC)

- P01 -

LONG-TERM OUTCOMES AFTER EUS-GUIDED PANCREATIC DUCT DRAINAGE. M. Van Haren (1), T. Aouattah (1), T. Moreels (1), R. Yeung (1), P. Deprez (1) / [1] Clin universitaires St-Luc, UCL, Brussels, Belgium, Gastroenterology.

Introduction: EUS-guided pancreatic duct drainage remains a niche indication for failed ERCP access to the pancreas. It is considered as one of the most challenging EUS drainage technique due to the underlying disease, anatomical variants, small caliber duct target, and unknown long-term efficacy.
Aim: To analyze the long-term clinical success of EUS-guided main pancreatic duct drainage (EUS-PD), and to find potential predictor factors for technical and clinical successes.
Methods: For this retrospective single tertiary-referral center study, data from patients with EUS-PD were collected in patient's charts and the endoscopy database, retrieving information on indication, technique of drainage, technical and clinical successes (total in case of no pain after treatment, and partial if more than 50% reduction in pain), adverse events, as well as reasons for failure defined as no improvement of (pain) symptoms, or need for surgery.
Results: A total of 66 patients were retrieved (62% male, median age 53y; range, 9-79) . EUS-PD was performed by transgastric (n= 40), transduodenal (n=4) approach, or by rendez-vous technique (n=21). Technical success was obtained in 82% (54/66), with an adverse event rate of 30% (20/66), of which one severe and 9 moderate (mostly pancreatitis and fluid effusions). Long-term clinical success was observed for 46 patients (n=46/54, 85.2%; total for 43 and partial for 3), during a median follow-up of 70 m (range 1-250). One or two stent exchanges were usually needed (median 1.7; range, 0-15). Three patients only underwent surgery. Higher clinical and technical success rates were associated with a large MPD diameter (p=0,008), and male gender (p=0,001). There was no significant relationship between the primary disease, drainage type, tobacco or alcohol use, and technical and clinical success rate.
Conclusions: EUS-guided pancreatic drainage is effective in the long term with a clinical success rate over 85%, and may therefore be considered as a good alternative to surgery. However, this technique is still challenging with 18% technical failures, even in an expert center.

- P02 -

INTRAVENOUS HEMIN, A POTENTIAL HEME OXYGENASE-1 ACTIVATOR, DOES NOT PROTECT FROM POST-ERCP ACUTE PANCREATITIS IN HUMAN: RESULTS OF A RANDOMIZED MULTICENTRIC MULTINATIONAL PLACEBO CONTROLLED TRIAL. R. Yared (1), C. Chen (2), A. Vandorpe (3), M. Arvanitakis (1), M. Delhaye (1), M. Fernandez Y Viesca (1), V. Huberty (1), D. Blero (1), E. Toussaint (4), A. Hittelet (5), D. Verset (6), W. Margos (6), O. Le Moine (1), H. Njimi (7), W. Liao (2), J. Devière (1), A. Lemmers (1) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, [2] National Taiwan University Hospital, Taipei, Taiwan (Province of China), Department of Internal Medecine, [3] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Pharmacy, [4] CHU de Charleroi, Hôpital Marie Curie, Charleroi, Belgium, Department of Gastroenterology, [5] CHU Ambroise Paré, Belgium, Department of Gastroenterology, [6] Centre Hospitalier de Jolimont-Lobbes, La Louvière, Belgium, Department of Gastroenterology, [7] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Intensive Care Unit.

Introduction: Data from basic research demonstrated that the activation of heme oxygenase (HO-1) by intraperitoneal administration of Hemin was effective in prevention and treatment of acute pancreatitis (AP) in mice models. This protective effect has been associated with intrapancreatic cytoprotective and anti-inflammatory macrophages recruitment. Knowing the lack of therapeutic phamacological target to treat AP in general, this molecular pathway was attractive as potential drug target in human.
Aim: We conducted a prospective randomized double-blind placebo-controlled trial to demonstrate a protective effect of Hemin administration to prevent post ERCP pancreatitis (PEP) in moderate risk patients.
Methods: In this multicenter, multinational, randomized, placebo-controlled, double-blind clinical trial, we assigned patients at moderate risk for PEP to receive a single IV dose of Hemin (4mg/kg) or placebo immediately after ERCP in a 1 :1 ratio. Patients were considered to be at moderate risk on the basis of validated patient (previous acute pancreatitis, normal bilirubinemia) and/or procedure-related (main pancreatic duct injection or guidewire insertion, biliary sphincteroplasty, precut papillotomy, pancreatic sphincterotomy) risk factors. No rectal NSAID was administered during the study. The insertion of prophylactic pancreatic stent was an exclusion criterion as well as sphincter of Oddi dysfunction, ampullectomy, known chronic pancreatitis, ongoing acute pancreatitis, pregnancy, Hemin allergy or severe kidney dysfunction. Blood samples were taken and pain was evaluated at 6h and next day after ERCP. Clinical contact was obtained by phone call for outpatients at 7 days. Randomization was performed by computer with blocks of 6 numbers transmitted between the central pharmacy and pharmacist of other centers. Opaque perfusion lines were prepared in a sterile environment and transmitted from the pharmacy to the endoscopy unit as soon as possible after the ERCP. The primary outcome was the incidence of PEP which was defined as new upper abdominal pain and an elevation of lipase to at least three times the upper limit of the normal range (ULN) within 24 hours after the procedure. Secondary outcomes evaluated lipase elevation, mortality, safety and length of stay. Sample size was calculated with a power of 80% to reduce PEP from 15 to 5%. 137 patients per group were needed. Ten supplementary patients per group were added for eventual dropoff. Final calculated sample size was 294 patients.
Results: From April 2012 to April 2021, a total of 281 of the 294 randomized patients had completed follow-up. Reason for drop-out were the following: ongoing acute pancreatitis before ERCP (4), pancreatic stenting during ERCP (2), drug administration technical problem (1), lost CRF or no follow-up (6). Indications for ERCP were choledocholithiasis (68%), benign biliary stricture (8%), malignant biliary stricture (18%), biliary leaks (4%) and others (2%). 141 patients received Hemin and 140 the placebo after a mean of 16 min and 15 min (p=0.565) from the end of the procedure, respectively. Groups were similar in terms of age, sex, indications, clinical and technical risk factors for PEP. ERCP duration was similar between groups (41.0 vs 41.2 min, p=0.648). PEP occured in 16 of 141 patients (11.3%) in the Hemin group and in 19 of 140 patients (13.6%) in the placebo group (p = 0.593). Severe PEP occurred in 1 patient (0.7%) in the Hemin group and in 5 patients (3.6%) in the placebo group (p = 0.12). Lipase elevation at more than 3x ULN did not differ between groups at 6 and 24h from ERCP. The mean duration of hospital stay was 4.8 days in the Hemin group and 4.7 days in the placebo group (p=0.784). The most common adverse event was phlebitis (14% in the Hemin group vs 3% with placebo (p=0.001)) Two deaths were reported in the Hemin group, one from severe sepsis secondary to cholangitis, the other from hemorragic shock related to esophageal variceal bleeding. There were no significant differences between the two groups concerning moderate or severe adverse events, or deaths at the end of follow-up.
Conclusions: Among patients at moderate risk for post-ERCP pancreatitis, intravenous Hemin injection does not protect from PEP when given after the procedure. This drug therefore seems of less interest to study in general acute pancreatitis management.

- P03 -

IRREVERSIBLE ELECTROPORATION IN THE MULTIDISCIPLINARY APPROACH OF PERIPANCREATIC TUMORS. AN INITIAL EXPERIENCE. J. Dubart (1), C. Bertrand (2), L. D'hondt (3), C. Schalbar (4), L. Faugeras (3), M. Mailleux (5), A. Dili (2) / [1] CHU-UCL-Namur site Godinne, Yvoir, Belgium, General surgery, [2] CHU-UCL-Namur site Godinne, Yvoir, Belgium, General surgery, [3] CHU-UCL-Namur site Godinne, Yvoir, Belgium, Oncology, [4] Centre Hospitalier du Nord, Ettelbruck, Luxembourg, Oncology, [5] Clinique Saint-luc Bouge, Namur, Belgium, Oncology.

Introduction: Irreversible electroporation (IRE) is a non-thermal ablative technology reported as exclusive treatment of locally advanced pancreatic cancer (LAPC) (in-situ IRE) or for margin accentuation (MA-IRE) in LAPC or in borderline resectable carcinomas (BRPC).
Aim: To report the initial, single-center, experience on feasibility, safety, and survival in patients treated with multimodal treatment for pancreatic malignancy including IRE.
Methods: From 2017 to 2020, 15 patients with non-metastatic pancreatic tumor were treated either by in-situ IRE (Group-A:9) or for MA-IRE combined to resection (Group-B:6). In-situ IRE indications: impossibility of R0-resection, patient unfit or refusing major resection. Oncologic and clinical parameters, morbidity, mortality, and overall survival were monitored. All patients suffering from pancreatic carcinoma (PC) received neoadjuvant chemotherapy.
Results: Although technically challenging, IRE was always feasible. Tumor classification: 2 resectable, 3 BRPC, 10 LAPC. Tumor distribution: pancreatic head 66,6%, isthmus 26,6%, tail 6,6%. Mean tumor diameter: 26,2mm (20-45mm). Mean age: 66yo (53-82), 73,3% Charlson Score ≥ 3. Combined IRE-surgery: Group-A: 2 hepaticojejunostomies, 1 surrenalectomy; Group-B: 4 Whipple; 2 splenopancreatectomies (1 Appleby procedure), 5 porto-mesenteric resections. No IRE-related perioperative complication. In hospital morbidity (Dindo-Clavien III): Group A: 11,1 %, Group-B: 50% (related to resection). Mortality occurred in 2 patients (Group-A), at 35 days due to angiocholitis-related multiorgan failure, and 78 days due to sudden death while on adjuvant chemoradiation. The median overall survival from diagnosis and IRE-treatment was respectively 23,6mo and 16,1mo. Recurrence free survival from diagnosis and from IRE: Group-A, 1 patient with BRPC (19,7mo and 15mo respectively); Group-B, 1 patient with BRPC (28,86mo and 24,9mo), and 1 patient with LAPC (20mo and 14mo). In the subgroup of LAPC median OS from diagnosis and from IRE-treatment is of 25,4mo and 17,7mo.
Conclusions: Our preliminary results suggest that IRE is a promising, low morbidity, technology for multimodal treatment of PC, offering survival benefit compared to current standard of care.

- P04 –

DUODENAL DUPLICATION CYST CAUSING RECURRENT ACUTE PANCREATITIS: CASE REPORT AND ENDOSCOPIC TREATMENT (WITH VIDEO). S. Lorea (1), R. Garces-Duran (2), T. De Grez (3), D. Blero (4) /

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Case Report: We report the case of a 33-year-old patient suffering from recurrent acute pancreatitis without common etiology. He complains since several years of recurrent, transfixing, abdominal pain localized in the epigastric region. He has no relevant medical history. The abdominal CT performed during an episode of acute pancreatitis showed an intraluminal 3cm cystic lesion localized in the second duodenum. The ultrasound-endoscopy showed an anechoic, submucosal lesion of cystic appearance, measuring 30 mm, located at the 2nd duodenum's internal face. The appearance of the mucosa was normal. The major papilla was also normal and located proximally to the lesion. At the MRI, biliary and pancreatic ducts end at the level of the major papilla and join the cystic lesion of the duodenal wall. The patient was treated endoscopically by section with a snare and marsupialization of the duodenal duplication cyst. The procedure was complicated by a local hemorrhage requiring endoscopic revision and placement of 2 clips. The histology confirmed the diagnosis by showing fragments of duodenal mucosa with preserved architecture lying on the muscularis on which, on the opposite side, mucosa of normal appearance was implanted. At one month follow up, the patient didn't present any recurrence of symptoms. This case illustrates an unusual pathology, the duodenal duplication cyst, a rare congenital malformation with an estimated prevalence less than 1 per 100,000 (1) which can leads to jaundice, acute pancreatitis or sometimes bleeding symptoms. The differential diagnosis included the choledochocele, the pancreatic pseudocyst and the ampulloma. (2) (3) Endoscopic resection is used and become a safe and effective alternative to surgery. We present here the videos of the endoscopic treatment of the patient. 1. Chen J-J, Lee H-C, Yeung C-Y, Chan W-T, Jiang C-B, Sheu J-C. Meta-analysis: the clinical features of the duodenal duplication cyst. J Pediatr Surg. 2010 Aug;45(8):1598–606. 2. Perrod G, Rahmi G, Samaha E, Vienne A, Cellier C. Duodenal duplication cyst: a rare cause of recurrent pancreatitis. VideoGIE. 2018 Feb;3(2):58–60. 3. Antaki F, Tringali A, Deprez P, Kwan V, Costamagna G, Le Moine O, et al. A case series of symptomatic intraluminal duodenal duplication cysts: presentation, endoscopic therapy, and long-term outcome (with video). Gastrointest Endosc. 2008 Jan;67(1):163–8.

- P05 -

LOOKING FOR THE NEEDLE IN A HAYSTACK. M. Vanhooren (1), S. Kindt (1) / [1] UZ Brussel, Jette, Belgium, Gastroenterology.

Case Report: A 71-year-old lady was sent to our tertiary endocrinology department for work-up of symptomatic hypoglycemia up to 40 mg/dL postprandial as well as after fasting. There was no history of diabetes mellitus, she was treated years ago with peroral and inhalation corticosteroids for asthma and underwent a Nissen fundoplicature for GERD in 2008. After factitious hypoglycemia or excessive alcohol consumption were excluded, a mixed-meal test and Synacthen test excluded respectively post Nissen dumping syndrome and adrenal insufficiency. A fasting glucose test was not suggestive for presence of insulinoma since there was no rise in insulin and c-peptide after fasting. Additionally, a glucagon stimulation test was negative. The work-up was completed with a PET-DOTATATE scan revealing no focal of diffuse enhanced serotonin receptor uptake. Finally, an echo-endoscopy of the pancreas revealed a small cystic lesion of the pancreatic body with subsequent distal pancreatectomy. Histopathology revealed no insulinoma but was suggestive for nesidioblastose, a rare form of Non-Insulinoma Pancreatogenous Hypoglycemia (NIPH) syndrome. Untill now the patient is cured from her hypoglycaemic spells.

WORKING GROUP OF DIGESTIVE PATHOLOGY (BELGIAN SOCIETY OF PATHOLOGY / BSP)

- R01 -

STROMAL PROLIFERATIONS IN GASTRIC INVERTED POLYPS ARE PLEXIFORM FIBROMYXOMA-LIKE RATHER THAN INFLAMMATORY MYOFIBROBLASTIC TUMOR-LIKE. L. Libbrecht (1), T. Billiet (2) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, pathology, [2] AZ Groeninge, Kortrijk, Belgium, Gastroenterology.

Case Report: Gastroscopy and echo-endoscopy in a 64-year-old man revealed the presence of a 1.8 cm diameter lesion in the mucosa/submucosa of the greater curvature of the stomach, which was clinically suspicious for a gastrointestinal stromal tumor or a leiomyoma. Fine needle aspiration cytology (FNAC) showed an ample amount of normal appearing foveolar structures and a stromal lesion with a morphological and immunohistochemical profile that seemed compatible with a gastric plexiform fibromyxoma. The lesion was resected and pathological analysis showed the picture of a gastric inverted polyp, hence explaining the extensive presence of foveolar structures in the FNAC, containing a stromal proliferation which was again reminiscent of a plexiform fibromyxoma. The stromal proliferation in this lesion consisted of spindle cells without atypia, embedded in a myxoid stroma rich in capillaries, sometimes with a plexiform aspect. The stromal cells were positive for alpha-smooth muscle actin and there was also multifocal to diffuse expression of CD10. Stainings for DOG1, CD117, ALK, desmine, cytokeratin, CD34 and synaptophysin were negative. Inflammatory cells, mainly lymphocytes, were only present in limited amount. The presence of stromal proliferations in gastric inverted polyps have been described previously, but these proliferations have always been considered to be inflammatory myofibroblastic tumor (IMT)-like (Noh, Pathol Int 2016 and Koh, Gastrointest Endosc 2019 and Kim, Am J Surg Pathol 2021). However, none of these studies performed immunohistochemistry for CD10, a marker for plexiform fibromyxoma which is negative in IMT, and in our view the images presented in these publications show a plexiform fibromyxoma-like rather than an IMT-like picture. Finally, plexiform fibromyxoma is a gastric-specific entity, while IMT usually presents in other organs and only rarely in the stomach, so it seems logical that stromal proliferations in inverted gastric polyp will mimic rather the former than the latter. In conclusion, we present a rare case of a gastric inverted polyp and we put forward that the stromal proliferations which are sometimes seen in this type of lesion are plexiform fibromyxoma-like rather than IMT-like.

- R02 -

POLYPOID COLON MUCOSA IN A LEUKEMIA PATIENT. I. Mariz (1), F. Lifrange (2), A. Van Gossum (3), L. Verset (1), D. Bron (4), M. Gomez-Galdon (1), P. Demetter (1) / [1] Institut Jules Bordet, Brussels, Belgium, Pathology, [2] CHU of Liège, Belgium, Pathology, [3] Institut Jules Bordet, Brussels, Belgium, Gastroenterology, [4] Institut Jules Bordet, Brussels, Belgium, Haematology.

Case Report: A woman with a history of chronic myeloid leukaemia (CML) reported digestive disorders and altered bowel habits upon a routine examination. Her medical history was marked by recurrent Helicobacter pylori gastritis and polymyalgia rheumatica. No other health issues were known. She was currently receiving dasatinib for CML and had hormone replacement therapy. Biology results remained normal and there was no anomaly in the leucocytic count. A colonoscopy was performed and revealed a colonic mucosa with an abnormal vasculature pattern and covered by multiple oedematous nodular lesions measuring less than 5 mm in diameter. This papular pattern reached all the way from the hepatic angle to the sigmoid. Staged biopsies were taken and sent for analysis. The histopathological examination of these nodules revealed discrete architectural distortions and a stroma containing a mixed inflammatory infiltrate composed of neutrophils, eosinophils and lymphocytes. There were no malignant or dysplastic cells. Immunohistochemistry for CD3, CD5, CD20 and CD79 did not bring arguments in favour of a lymphoma. Based on these endoscopic and histopathological findings, the diagnosis of a dasatinib induced colitis (DIC) was suggested. The dasatinib treatment was stopped. Once stopped, the patient's digestive symptoms disappeared, and a control colonoscopy performed five weeks later revealed a colon with no macroscopic anomalies. Subsequent biopsies of the colon revealed a strictly normal mucosa with no signs of atypia nor excess inflammatory cells. Tyrosine kinase inhibitors are currently the main treatment options for CML. Although imatinib is widely accepted as being the first-line treatment of CML, some second-generation drugs (such as nilotinib and dasatinib) can be administered in the frontline settings. Dasatinib can be used in first or second line treatment of patients with CML and is particularly useful in the case of patients who develop an imatinib resistance. The most common adverse effects of dasatinib are usually well tolerated. These include myelosuppression, transaminitis, fluid retention and gastrointestinal disorders such as nausea and diarrhoea. Lower gastro-intestinal haemorrhage has been reported in 2-9% of cases. Even if well described in literature, dasatinib induced colitis (DIC) remains an uncommon side effect which typically appears weeks to months after the initiation of dasatinib under the form of bloody diarrhoea. In the majority of cases drug therapy must be interrupted, reduced or switched to another tyrosine kinase inhibitor. We share this case to draw attention to the fact that dasatinib induced colitis can also appear paucisymptomatic or asymptomatic, even in presence of worrisome endoscopic findings.

- R03 -

ASEPTIC LIVER ABSCESSES IN NEWLY DIAGNOSED CROHN'S DISEASE. C. Vuckovic (1), A. Cremer (1) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology.

Case Report: A 18-year-old woman, living in Belgium, presented at the Internal Medicine outpatient clinic with nonspecific abdominal pain and intermittent fever for the last 6 weeks. Her past medical history was unremarkable except that she was recently diagnosed with an irritable bowel syndrome, based on intermittent flat stools and crampoid abdominal pain. Clinical examination showed slight epigastric pain, erythema nodosum and mouth aphtosis. Laboratory tests revealed a biologic inflammatory syndrome with anemia (10g hemoglobin/dL), mild neutrophilia (10 000 polynuclear neutrophils /µL), moderate thrombocytosis (640 000 platelets/µL) and elevated C-reactive protein (CRP) (120mg/L) and ferritin levels (327 mg/L). Urine, stool and blood cultures were negative, as well as multiples serologies. Faecal calprotectin was elevated at 412µg/g faeces. Thoraco-abdominal computed tomography scan showed a slight hepatomegaly. Small intestine imaging was in favor of terminal ileitis. Upper and lower digestive tract endoscopies were performed and showed mostly aphthous lesions in the oesophagus and the gastric antrum. Lower digestive tract was macroscopically unremarkable, though histological analysis confirmed nonspecific ileitis and pancolitis as well as gastritis with one single antral non necrotic granuloma. Corticoids were initiated for a strong suspicion of Crohn's disease, sarcoidosis being the main differential diagnosis, with clinical and biological improvement of the CRP levels (19 mg/L). Three weeks after the end of the corticotherapy, she was hospitalized for fever and right upper quadrant pain with a diagnosis of multiple liver abscesses of unknown origin. Laboratory tests revealed an elevated CRP level (210 mg/L) and the sudden onset of a cholestasis with elevated gamma-glutamyl transferase (431 U/L) and alkaline phosphatase (361 U/L). Transaminases were normal. A transcutaneous hepatic biopsy was performed with microbiological and histological samples. Large spectre antibiotherapy was then initiated for 10 days with persistent fever and elevated biological inflammatory syndrome as well as new onset of coagulopathy (prothrombin time: 44%). Histology showed nonspecific lesions and microbiology of the abscesses and blood cultures were negative for bacterial and mycobacterium infection. Given those results, due to high suspicion of aseptic abscesses as extra digestive manifestation of Crohn's Disease, corticotherapy (intravenous methylprednisolone 0.8mg/kg) was initiated with fast clinical and biological major improvement, followed by infliximab infusions. The coagulopathy quickly resolved as well as the cholestasis. Hepatic MRI showed a resolution of the lesions 4 weeks after initiation of the treatment. Aseptic abscess is a rare extra-digestive manifestation of inflammatory bowel disease whose diagnosis is challenging due to its very low prevalence as well as its presentation in immunocompromised patients prone to infectious complications.

- R04 -

DURING THE COURSE OF THE DISEASE, IBD-PATIENTS MAY PRESENT WITH DIFFERENT COMPLICATIONS. A. Vandendriessche (1), A. Jauregui-Amezaga (2), S. Van Den Broeck (3), A. Driessen (1) / [1] University Hospital Antwerp, Edegem, Belgium, Pathology, [2] University Hospital Antwerp, Edegem, Belgium, Gastroenterology and Hepatology, [3] University Hospital Antwerp, Edegem, Belgium, Surgery.

Case Report: Inflammatory bowel disease is a chronic and relapsing inflammatory disorder, involving different segments of the gastrointestinal tract. This disease, which comprises Crohn's disease and ulcerative colitis, varies in extent and severity over time. Several cohort studies have shown that the behavior of Crohn's disease may vary in time. At diagnosis, patients most commonly present with symptoms of inflammation, but during follow-up, disease behavior may change to a penetrating or stricturing phenotype. During the course of the disease nearly two third of the patients develop complications. The nature of these complications varies in function of time and course of the disease. Our case involves a 51-year-old male, diagnosed with Crohn's disease. Originally symptoms were mild, but over time the patient presented with severe crampy pain suspicious for a subobstruction. Despite symptomatic treatment, the symptoms kept on recurring, so the patient underwent surgery with resection of the involved intestine. Gross examination revealed not only a narrowing of the intestine, but part of the inflamed mucosa had an unusual appearance. Microscopical examination revealed an unusual inflammatory pattern at the mucosa of the intestine. In the deeper layers of the wall inflammatory and connective tissue changes were observed, responsible for the narrowing of the intestine. Our case demonstrates a range of complications that developed during the course of its disease. In Crohn's disease these complications differ over time and disease behavior. At the time of severe disease activity, patients are at risk of different infections, e.g. viral and parasitic infections. The increased risk of infections is not only due to the altered microbiome in the inflamed mucosa, but also the result of the application of antibiotics and immunosuppressive drugs. Due to these infections, inflammation may even progress to a fulminant colitis. Whereas ulcerative colitis is more or less restricted to the mucosa, Crohn's disease involves different layers of the intestine, resulting in transmural inflammation. The deeply infiltrative inflammation may induce the development of fistulae. Other complications are strictures, of which the treatment may vary in function of the nature of the stricture. During the long course of the disease, patients may also develop late complications, such as dysplasia and IBD-related cancer. Different types of complications may arise during the course of the disease in IBD-patients. Awareness is important, seeing the complications like a surinfection may influence symptoms as well treatment. Additionally, frequent endoscopic surveillance with sampling of tissue biopsies is necessary to detect the preneoplastic lesions and IBD-related cancer at an early stage.

- R05 -

STRONGYLOIDES STERCORALIS HYPERINFECTION SYNDROM MIMICKING SEVERE ACUTE COLITIS. M. Zeriouh (1), C. Liefferinckx (2), G. Englebert (2), M. Abdessalami (2), A. Cremer (2) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Brussels, Belgium, Gastroenterology, [2] Erasme University Hospital - Université Libre de Bruxelles (ULB), Brussels, Belgium, Gastroenterology.

Case Report: A 36-year-old African man, living in Belgium for years, presented to the emergency department with recent weight loss of 10 kg and a 7-days history of abdominal pain, rectal bleeding, and diarrhea. He has a significant past medical history of Ulcerative Colitis (UC) diagnosed in 2012 and currently treated with tofacitinib 10 mg twice daily. He has been treated with corticosteroids twice in the past six months for UC flares. His last travel abroad was two years ago. There is no tobacco or alcohol consumption. Initial lab results showed a high leukocyte count (13,000/mm3), eosinophilia (1340/ mm3), anemia (7,3g hemoglobin/dl) and C-reactive protein of 22 mg/L. Abdominal computed tomography scan showed parietal thickening of the colon with the presence of a left posterior para-anal abscess of 4 cm long axis. Tofacitinib was stopped, antibiotherapy started and abscess drainage performed. Additional assessment by gastroscopy and colonoscopy was done. Gastroscopy showed erythematous mucosa and diffuse hyperhemia with superficial non-hemorrhagic erosions at the antrum, as well as diffuse whitish deposit at the antrum and the duodenum. Left coloscopy revealed two superficial ulcer of 1 cm in the sigmoid with a Mayo endoscopic subscore of 3. Histological examination of the antrum, stomach body, duodenum and colon showed massive strongyloides infestation with acute inflammatory lesions of the colonic mucosa containing numerous eosinophilic leukocytes and a reaction mixed leukocytes (mono- and polynuclear leukocytes). Small calcified structures that may correspond to parasitic eggs were isolated. Serology was positive for strongyloides stercoralis. The patient was treated with ivermectine for 10 days allowing clinical and biological improvement. Three months later, colonoscopy showed endoscopic remission with Mayo endoscopic subscore of 0 under mesalasine 2 g once daily. Flare of inflammatory bowel disease is usually treated with corticosteroids which has been proven to be the leading risk factor for the most severe forms of strongyloidiasis. Although it is a rare entity in our country, the correct diagnosis and treatment of Strongyloides hyperinfection syndrom is of critical importance to avoid UC treatment escalation (including colectomy) as it is a life-threatening disease.

- R06 -

CHRONIC ILEITIS, A CHALLENGING DIAGNOSIS FOR THE PATHOLOGIST. A. Francois (1), A. Wabik (1), H. Dano (1), O. Dewit (2), A. Kartheuser (3), A. Jouret-Mourin (1), P. Baldin (1) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Pathology, [2] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Gastroenterology, [3] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Colorectal Surgery Unit.

Introduction: In Belgium, the main cause of chronic ileitis is Crohn's disease (CD). Endoscopic features of CD are not specific and may overlap with other less common diseases. The histological evaluation may help improve the diagnosis. We would like to present a case highlighting the importance of considering the differential diagnosis of rare intestinal disorders when assessing chronic ileitis. We would also like to put emphasis on the importance of active collaboration with clinicians as a key for the best management of our patients.
Materials and methods: A 17-year-old boy presented with abdominal pain, constipation and weight loss. Clinically, the suspected diagnosis was CD. He underwent a lower and upper GI endoscopy, which showed inflammation in the distal ileum compatible with Crohn's disease. Ileal biopsies showed a diffuse chronic inflammatory infiltrate without typical features of Crohn's disease. Due to the clinical aggravation of the patient, an ileocecal resection was required. The pathological evaluation of this sample lacked the diagnostic criteria of CD but showed the presence of perivascular inflammation, vasculitis, superficial ulcers and vessel thrombi suggesting Behçet's vasculitis.
Conclusion: Diagnosis of CD mimickers could be challenging due to the discrepancy between clinical, endoscopical and histological features. These diseases are rare but the pathologist needs to keep them in mind when making a diagnosis, furthermore based on a biopsy specimen.

- R07 -

SEXUALLY TRANSMITTED INFECTIOUS COLITIS, A MIMICKER OF INFLAMMATORY BOWEL DISEASE. J. Fallas (1), M. Bortes (2), P. Eisendrath (3), P. Demetter (1), L. Verset (1) / [1] Institut Jules Bordet, Brussels, Belgium, Pathology, [2] Hôpital Saint-Pierre, Belgium, Gastroenterology, [3] Hôpital Saint-Pierre, Bruxelles, Belgium, Gastroenterology.

Case Report: Sexually transmitted infectious colitis often raises concern for inflammatory bowel disease (IBD) as it shares many overlapping clinical and histological features. The two most common causative agents are Treponema pallidum and Chlamydia trachomatis. In this example, we describe a case of primary rectal syphilis, which was diagnosed on the biopsy specimens.
A 40-year-old man presented with a two weeks history of rectal bleeding and tenesmus. He mentioned having sex with men and that evaluation for HIV and other sexually transmitted diseases had last been performed more than a year ago. Digital rectal examination revealed the presence of a 3 to 4 cm mass, on the anterior wall of the rectum, 5 cm above the anal margin. A rectoscopy was carried out and confirmed the presence of a single nodular mass, with an ulcerated and crumbly surface. Biopsy samples were collected in order to characterise the lesion. Screening for sexually transmitted diseases was performed concomitantly. Biopsy specimens showed fragments of a rectal mucosa in which the lamina propria was the seat of a granulation tissue characterized by a dense inflammatory infiltrate mainly composed of plasma cells. The glandular architecture was globally preserved. No crypt distortion nor cryptitis was observed. Immunohistochemical staining for CD-138 confirmed the prominent plasma cell infiltrate and Treponema pallidum stain revealed strong and diffuse positivity within the lesion. The result of the treponemal antibody test came back positive, supporting our diagnosis. The patient was treated with intramuscular penicillin injections. The case illustrates the similarities and discrepancies between the clinical and histological presentation of sexually transmitted infectious colitis and IBDs. Sexually transmitted infectious colitis should always be considered in the differential diagnosis of anal canal ulcers, anorectal inflammatory masses and proctitis, particularly in men who have sex with men. Immunohistochemical staining for Treponema can help avoid misdiagnosis, which could lead to disease progression and late diagnosis.

- R08 -

THE GREAT BUT RARE MIMICKER. M. Vanhooren (1), M. Surmont (1), S. Francois (1), S. Kindt (1) / [1] UZ Brussel, Jette, Belgium, Gastroenterology.

Case Report: We present a case of a previously asymptomatic middle-aged man, known for diverticulosis, Binet A chronic lymphatic leukemia and psoriatic arthritis, who is admitted at the gastro-enterology department for 5 weeks lasting bloody diarrhea associated with a 33lbs (15kg) weight loss. At admission, his abdomen is diffusely tender by palpation and slightly distended without signs of systemic toxicity. CT scan reveals a pancolitis with involvement of terminal ileum and prominent vascular congestion. There are no signs of perforation. On initial flexible rectosigmoïdoscopy, rectosigmoïditis with ulcerative proctitis and negative biopsies for ischemia, inflammatory bowel disorder, neoplasia, CMV, TBC and spirochete is seen. Fecal cultures for c. difficile, classic enteropathogens, Giardia and Cryptosporidium are negative. Broad spectrum antibiotics are started and by means of additional histologic evidence a new ileocolonoscopy is undertaken few days later. There is no change in endoscopic appearance with diffuse colonic erythema and edema hampering progression beyond the splenic flexure. In suspicion of acute severe ulcerative colitis (ASUC) high dose intravenous corticosteroids are initiated. Three days later the patient deteriorates with absent bowel sounds, aggravating pain symptoms and pneumoperitoneum on CT scan, suggestive for colonic perforation ultimately leading to subtotal colectomy with protective ileostomy. Examination of the pathology specimen reveals circumferential ulceration with scarring, a thickened venous wall with active inflammation and fibrotic changes that consequently produce obstruction of the venous lumen in the subserosa. A diagnose of Idiopathic myointimal hyperplasia of mesenteric veins (IMHMV) is made, a very uncommon and poorly understood ischemic disease affecting mainly the rectosigmoid colon of relatively young, otherwise healthy males. It is a great mimicker of IBD, only diagnosed on histopathology of resected perforated colon specimens after failed therapy lines. There is no known treatment for IMHMV but fortunately IMHMV patients whose affected colon has been resected appear to be cured, with no recurrence of disease-related activity or symptoms as is the case for this patient.

- R09 -

DYSPLASIA IN CROHN'S DISEASE: AN INFREQUENT DIAGNOSIS, NOT TO MISS. A. Sieben (1), A. Vandendriessche (1), E. Baetens (1), N. Komen (2), M. Somers (3), A. Driessen (1) / [1] Antwerp University Hospital, Edegem, Belgium, Pathology, [2] Antwerp University Hospital, Edegem, Belgium, Abdominal Surgery, [3] Antwerp University Hospital, Edegem, Belgium, Gastroenterology and Hepatology.

Case Report: Due to the continuous inflamed state of the mucosa, ulcerative colitis and Crohn's disease patients are at risk of developing colorectal cancer at an earlier age and with a poorer prognosis. The incidence of IBD-related cancer is 2%. The risk of cancer is determined by patient-related factors such as a family history of sporadic colorectal cancer, a first-degree relative with colorectal cancer before the age of 50 years, primary sclerosing cholangitis in ulcerative colitis patients, and disease-related factors such as early onset of inflammatory bowel disease, the extent, severity, and duration of the colitis. Hence continuous surveillance, initiated 8 to 10 years after the beginning of the inflammatory process, is necessary to detect the preneoplastic lesions in an early stage. New endoscopic techniques have improved the diagnostic accuracy of dysplastic lesions and have resulted in a new and more simplified classification system of these lesions in the bowel. We present the case of a 52-year-old patient with right-sided Crohn's disease, diagnosed at the age of 49 years. Consecutive surveillance ileocoloscopies showed right sided colitis with skip lesions at the level of the colon transversum and colon descendens. Standard endoscopic examination revealed no lesions, suspicious for malignancy. Random sampling of the ileum and the different segments of the colon however showed an inflamed mucosa with low grade dysplasia in the caecum. Detection of dysplastic lesions during standard endoscopic examination should be confirmed by other endoscopic methods with a higher diagnostic accuracy, such as chromo-endoscopy. The improvement of endoscopic techniques has resulted in a change of the diagnostic approach with random or target biopsies of these lesions in function of their visibility. Based on the improved visibility of these lesions, a new and more simplified classification system is developed. Not only in function of their visibility but also of their resectability the therapeutic approach of these dysplastic lesions will vary, as demonstrated in our case.

- Y01 -

HEMOLYTIC ANEMIA & CIRRHOSIS: ABOUT A CASE. S. Ziane Bouziane (1), C. Lelubre (2), W. Soub Defeu (3), J. Cofino Casanueva (2), V. Chua (4) / [1] CHU de Charleroi, Hôpital Marie Curie, Charleroi, Belgium, Internal medecine, [2] CHU de Charleroi, Hôpital Marie Curie, Charleroi, Belgium, Internal medecine, [3] CHU de Charleroi, Hôpital Marie Curie, Charleroi, Belgium, Gastroenterology, [4] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, Internal medicine.

Case Report: Acute anemia is a frequent reason of consultation and admission into emergency services. In cirrhotic patients, anemia is often chronic, multifactorial and with a complex physiopathology. The aim of this case report is to highlight the practical difficulties of differential diagnosis and etiological workup of hemolytic anemia in cirrhotic patients. We present the case of a 48-year-old man who presented to the hospital with increasing asthenia for two weeks. The patient is known to have exogenous cirrhosis classified as Child C 10, hypertension and peptic ulcer. The blood count on admission showed significant anemia (hemoglobin level: 6.8 g/dl (MCV: 107 fl, reticulocytes: 156.7/mm³), predominantly unconjugated hyperbilirubinemia: 19.41 mg/dldl, elevated lactate dehydrogenase level: 428 U/L and a collapsed haptoglobin level <0.3. The patient received an urgent transfusion of two units of packed red blood cells, with a low post-transfusion yield. Based on these elements, a diagnosis of hemolytic anemia was quickly made. The results of the admission biology are detailed below. A schizocyte test was performed and came back negative, as well as a cold agglutinin test and the viral serologies (HAV, HBV, HCV, EBV, CMV, HIV, Rubella, syphilis, parvovirus B19). Vitamin levels (folic acid, vitamin B12) and ferritin levels were normal. A bone marrow aspiration with cytological and immunohistochemical analysis was performed and returned normal. The final diagnosis was obtained by performing a manual peripheral blood smear. Acanthocytes were identified and represented more than 20% of the red blood cells. Our patient received several transfusions since his hospitalization. He died of hemorrhagic shock four months after the discovery of acanthocyte anemia. Spur cell anemia is an acquired form of corpuscular pathology of the red blood cell responsible for hemolytic anemia. Acanthocytes, or spur cells, are deformed red blood cells with irregular projections of the cytoplasmic membrane, and are characterized by a reduced half-life due to increased splenic sequestration and destruction. Although the physiopathology is not fully elucidated, it appears that this characteristic membrane deformation is secondary to a decrease in the hepatic capacity to esterify cholesterol (by a decrease in the activity of the serum's lecithin-cholesterol acetyltransferase), leading to its incorporation into the phospholipid membrane layers of erythrocytes, and causing an irreversible rigidification of the cytoplasmic membrane. Acanthocytes, although not specific of cirrhotic states, are indicative of advanced liver disease and represents a criterion of severity with a high mortality rate in the year following diagnosis. The prevalence of acanthocytosis in cirrhotic patients remains poorly documented, and the differential diagnosis is essentially composed of Zieve 's syndrome, a form of hemolytic anemia of the cirrhotic patient associated with jaunice and hyperlipemia, essentially related to ethanol toxicity on the erythrocyte membrane and classically not including acanthocytes on the blood smear. In this case, liver transplantation remains the only effective treatment of anemia, a disappearance of acanthocytes having been described in post transplantation. Apart from liver transplantation, a treatment associating flunarizine, pentoxifylline and cholestyramine has been described in a few published cases without significant results, plasmapheresis while waiting for transplantation has been used in a few cases reported in the literature. Acanthocyte anemia is not an uncommon cause of anemia in cirrhotic patients, but it is not frequently mentioned in current practice. This example highlights the importance of looking for acanthocytosis in presence of hemolytic anemia in cirrhotic patients and the crucial role of the peripheral blood smear in the diagnostic process, an inexpensive and reproducible procedure. Admission Biological Results: GB (4.0-10.5 10³ /mm³) 3.05. Hg (11.1-14.6 g/dL) 6.8. Hct (33.2-43.4%) 17.9. MCV (80-100 fL) 107. Plt (140-400 10³ /mm³) 33 Sodium (135-146 mmol/L) 136. Potassium (3.5-5.5 mmol/L) 6. Chlorine (98-110 mmol/L) 100. Bicarbonate (19-34 mmol/L 26. Urea (6-20 mg/dL) 79. Creatinine (0.4-1.1 mg/dL) 1.08. Total bilirubin (0-1.2 mg/dL) 19.41. Indirect bilirubin (0.0-0.3 mg/dL) 5.08. Albumin (3.5-5.2 g/dL) 3.58. GOT (5-34 U/L) 83. GPT (<55 U/L) 25. Alkaline phosphatase (40-150 U/L) 108 Vitamin B12 (138-652 pmol/L) 1118. Folate (3.1-20.5 µg/L) 4.9. Iron (65-175 µg/dL) 209. TIBC (250-400 µg/dL) 234. Ferritin (22-247 µg/L) 450. Transferrin (1.74-3.64%) 1.71. Reticulocytes /mm³ 156.7. LDH (135-214 U/L) 428. Indirect Bilirubin mg/dl 14.33. Haptoglobin g/dL<0.03.

- Y02 -

NON-ALCOHOLIC STEATOHEPATITIS AND BARIATRIC SURGERY: AN UNWARRANTED IMPROVEMENT. I. Delaleeuwe (1), J. Aoun (1), T. Sersté (1), J. Mulkay (1), A. Hoyois (1), A. Cuvelier (2), P. Eisendrath (1) / [1] CHU Saint-Pierre, Brussels, Belgium, Gastroenterology and Hepatology, [2] CHU Saint-Pierre, Brussels, Belgium, Nutrition.

Case Report: A 55-year-old female patient with morbid obesity (weight [W] 93 kg, length [L] 152 cm, body mass index [BMI] 40 kg/m2) was suffering from metabolic syndrome. She underwent a laparoscopic gastric bypass in 2014 and lost eventually 14 kilograms. Due to persistent reflux symptoms post operatively, a surgical tightening of the diaphragmatic hiatus was attempted in February 2021 followed by a surgical revision of the gastro-jejunal anastomosis in April 2021. The patient's daily nutritional intake significantly decreased after the revision surgeries, to be estimated at approximately 100 kcal a day. She presented in August 2021 to the emergency department for abdominal pain, anorexia and weight loss of 10 kg (12 % of total body weight [TBW], i.e. W of 71 kg) over the last 4 months. Clinical examination revealed jaundice and tenderness in the right hypochondrium. There was no sign of hepatic encephalopathy. Laboratory results showed a decrease of PT to 40.0 %, an elevated total bilirubin level of 6.3 mg/dL, an elevated GGT of 674 UI/L, slightly elevated transaminases level (AST of 156 UI/L and ALT of 36 UI/L) and a low albumin level of 21 g/L. Abdominal ultrasound disclosed a slight amount of ascites and no obvious biliary dilation. No biliary obstacle or cholecystolithiasis could be detected on abdominal contrast enhanced CT nor MRCP. The abdominal CT-scan showed hepatomegaly of 21 cm and a liver attenuation of 14 Hounsfield Units compatible with severe steatosis. The distal bile ducts were not visible by EUS due to the anatomical post-gastric bypass state, but the absence of intrahepatic bile duct dilatation was confirmed. A liver biopsy was performed and showed diffuse steatosis, hepatocyte ballooning and Mallory bodies in the liver parenchyma. A neutrophilic infiltration was shown in the portal tracts. There was no evidence of neo ductular proliferation. The fibrosis was severe with multiple septa formations. Findings were compatible with the diagnosis of non-alcoholic steatohepatitis (NASH), classified as A4F3 with severe steatosis according to the Brunt classification. The vast majority of clinical studies in literature highlighted on the favorable effects of weight loss post bariatric surgery on non-alcoholic fatty liver disease (NAFLD) and NASH, and the potential regression of preoperative hepatic fibrosis. This case illustrates a rare impairment of liver function after bariatric surgery, notably gastric bypass, with malnutrition as the main pillar. The possible pathophysiological mechanism behind the hepatic impairment seen in this case is the combination of severe protein-caloric deficit, small intestinal bacterial overgrowth (SIBO) and lipotoxicity. Malnutrition and SIBO can be addressed as potential targets for treatment. The management should be based on a multidisciplinary approach involving hepatologists, surgeons, and nutritionists. Enteral nutrition through a nasojejunal tube and protein supplementation was initiated for our patient reaching a target of 1750 kCal/day in a progressive manner in order to prevent a refeeding syndrome. An intestinal decontamination by rifaximine 550 mg twice a day for 28 days was started. Favorable evolution of liver enzymes (total bilirubin of 1.9 mg/dL), increase of PT >50 % and albumin (31 g/L) was seen after 7-10 days of treatment.

- Y03 -

RECURRENT MYCOPLASMA PNEUMONIAE INFECTION CAUSING HEPATITIS AND CHOLESTASIS IN A YOUNG GIRL. E. Levy (1), Y. Vandenplas (2), K. Huysentruyt (2), E. De Greef (2) / [1] CHU Saint-Pierre, Brussels, Belgium, Paediatric gastroenterology, [2] UZ Brussel, Jette, Belgium, KidZ Health Castle, Paediatric gastroenterology.

Case Report: We present a case of a five-year-old girl with recurrent episodes of hepatitis and cholestasis associated with mycoplasma pneumoniae infection. A previously healthy child presented at the age of 4 years a first time with cholestasis (icterus, pruritus), polydipsia and polyuria. Blood results showed: normal glycemia, alanine aminotransferase (ALAT) 90 U/L (0-33 U/L) / aspartate aminotransferase (ASAT) 123 U/L (0-41 U/L), gamma-glutamyl transferase (ɣGT) 45 U/L (4-12 U/L), total bilirubin 2.87/ mg/dl (0-1.2 mg/dl), direct bilirubin 2.4 mg/dl (0-0.3 mg/dl), C-reactive protein (CRP) 1.2 mg/L (< 5mg/L), white blood cells 23500 mm3 (3500-12000 mm3), neutrophils 9188 (1800-6800 mm3) lymphocytes 10928 mm3 (1500-5500 mm3). Hepatitis B (protected), C and A, Epstein-Barr (EBV) virus and cytomegalovirus (CMV) serology were negative. Mycoplasma pneumoniae titer was positive (320 (positive if >160). A more elaborated work-up was performed: alfa-1-trypsin, organic acids, catecholamines, ceruloplasmin, iron, autoimmune diseases (anti-neutrophil cytoplasmic, anti-nuclear, smooth muscle and anti–liver-kidney microsomal antibodies), ferritin and alpha-foetoprotein were all normal. She was treated with clarithromycin 20 mg/kg/day for five days and symptoms rapidly disappeared allowing to stop the drugs that were started for icterus/pruritus (Desloratadine 5 mg/day, Questran 4 gram/day and 150 mg ursodeoxycholic acid 3x/day). The girl was lost in follow-up due to the COVID lockdown; normalisation of the cholestasis and transaminases could not be documented. Exactly one year later, she presented again with exactly the same symptoms: icterus, pruritis, polydipsia and polyuria. Blood results showed similar abnormalities: normal glycemia, ALAT 445 U/L, ASAT 200 U/L, ɣGT 66 U/L, total bilirubin 1.62/ mg/dl, conjugated bilirubin 1.42 mg/dl, CRP 1.0 mg/L (< 5mg/L), white blood cells 18400 mm3 and lymphocytosis 12144 mm3 Hepatitis B, C and A serology was negative. EBV virus IgG 48.97 (positive if ≥1,00), and IgM 6.59 (positive if ≥1,00:) were positive and CMV titer IgG was 0 and IgM 1.77 (positive if ≥1,00:). Mycoplasma pneumoniae titer was also positive, with a much higher titer as during the first episode (2560). As mycoplasma serology could stay elevated for a longer period, we considered this second episode possibly linked to CMV. Abdominal ultrasound was normal. Genetic screening for cholestasis and recurrent cholestatis panel was negative. We treated her for the cholestasis and itchiness with antihistaminics (Desloratadine 5mg/day) and ursodeoxycholic acid (150mg/day) together with a topical cooling cream. Because cholestasis was increasing (total bilirubin 2.87 mg/dl, conjugated bilirubin 2.75 mg/dl) and transaminase were stable, but itching persisted, rifampicin was added to the treatment. She refused Questran. After a month of treatment, the symptoms persisted as did the cholestasis (total bilirubin 3.11/ mg/dl, direct bilirubin 3.11 mg/dl) (ALAT 475 U/L/ ASAT 244 U/L). We decided to start Clarithromycin 20mg/kg/day for five days because. EBV/CMV viral load were known in the meantime and negative. Within one week she was completely asymptomatic, just as during the first episode. Further, within a month she had

a normal laboratory testing, except for Mycoplasma serology that increased up to 1:5120 two months after the onset of symptoms. Only five other case reports describe a primo-infection with mycoplasma pneumoniae causing hepatitis with(out) cholestasis. We present a case of a recurrent Mycoplasma induced hepatitis and to our knowledge this has never been reported previously. Mycoplasma is a rare cause of cholestasis in children and should be recognized early to enable adequate and early treatment

- Y04 -

INTRAHEPATIC CHOLANGIOCARCINOMA WITH PREDOMINANT DUCTAL PLATE MALFORMATION PATTERN: AN UNUSUAL MIMICKER OF BENIGN LESION. F. Noel (1), O. Detry (2), C. Sampoux (3), N. Blétard (1) / [1] CHU of Liège, Belgium, Anatomie pathologique, [2] CHU of Liège, Belgium, Abdominal Surgery, [3] CHUV Lausanne, Lausanne, Switzerland, Pathology Department.

Case Report: Background Intrahepatic cholangiocarcinoma with predominant ductal plate malformation pattern is a recently discovered rare entity. This lesion has similar histological features seen in a ductal plate malformation, which resembling ductular reaction and would be developped from hepatic progenitor cells. Materials, methods and results A 57-year-old woman presented a liver mass in the right lobe. A diagnosis of biliary adenofibroma was suggested on the first biopsy. In a second stage, a right hepatectomy was performed. On gross examination, we found a lesion 5,5 cm long, whitish, firm, well-demarcated, homogeneous, located within segment 7. On histology, this lesion was unencapsulated and pushing out the rest of the non-tumorous liver parenchyma. The tumour is characterised by a scattered well-differentiated ductular proliferation within a dense fibrous stroma. Glandular structures with irregular dilated lumens are lined by a low-colmunar-to-cuboidal cells with high nucleocytoplasmic ratios and round vesicular nuclei. There was no marked pleomorphism. Usually, no mucin is visualised. Some immunohistochemistry was realised, Arginase 1, Hep-Par1 and S100 were negative. All tubules expressed CK7 and CK19 heterogeneously. EMA demonstrated an apical diffuse marking on tumor cells. EPCAM revealed an extended basolateral positivity and NCAM, a partial basolateral positivity. Immunohistochemistry for P53 was wild-type. The proliferation index assessed by ki67 was low, around 5%. Finally, a diagnosis of intrahepatic cholangiocarcinoma with predominant ductal plate malformation pattern was retained. Conclusion Intrahepatic cholangiocarcinoma with predominant ductal plate malformation pattern is an unusual entity that can mimic a benign lesion.

- Y05 -

AUTOIMMUNE HEPATITIS DEVELOPING AFTER SARS-COV-2 VACCINATION: SERIES OF THREE CASES. G. Rasschaert (1), S. François (1), A. Verbeeck (2), M. Schils (1), M. Aerts (1), P. Lefesvre (3), I. Colle (4), H. Reynaert (1) / [1] Universitair Ziekenhuis Brussel, Brussels, Belgium, Gastroenterology and Hepatology department, [2] Algemeen Stedelijk Ziekenhuis Aalst, Aalst, Belgium, Gastroenterology and Hepatology department, [3] Universitair Ziekenhuis Brussel, Brussels, Belgium, Pathology department, [4] Universitair ziekenhuis Gent, Belgium, Gastroenterology and Hepatology Department.

Case Report: We present a series of three patients with an assumed diagnosis of autoimmune hepatitis (AIH) after SARS-CoV-2 vaccination. A 57-year-old woman was referred for progressive elevation of liver function tests (LFTs) four weeks following the first dose of Moderna mRNA-1273 vaccination. Medical history included Hashimoto's thyroiditis and SARS-CoV-2 infection six months earlier with a mild disease course. She did not take medication or herbal supplements. No substance abuse was recorded. LFTs were normal one month before vaccination. Physical examination was unremarkable. At referral, laboratories were significant for aspartate aminotransferase (AST) (22xULN), alanine aminotransferase (ALT) (38xULN), alkaline phosphatase (AP) (1.3xULN) and gamma-glutamyl transpeptidase (GGT) (3xULN). Hepatitis A, B, C and E virus markers, HIV, Cytomegalovirus, Epstein-Barr, Herpes simplex type 1 and 2 serology were negative. Ceruloplasmin and α1-antitrypsin levels were normal. Anti-mitochondrial, anti-smooth muscle, anti-liver-kidney microsomal antibodies were negative, while antinuclear antibody (ANA) was positive (1:320, speckled pattern). Total IgG was normal. Abdominal ultrasound was unremarkable. Histology showed interface activity including a mixed inflammatory infiltrate with predominant lymphocytes, focal rosetting was observed. According to the International Autoimmune Hepatitis Group (IAIHG) criteria, pre-treatment score was 19, accounting for definite AIH. Immunosuppression was not immediately started due to slow but progressive decrease of LFTs. However, six weeks later budesonide 9mg was initiated for an increase in LFTs (transaminases x10 ULN). Lack of efficacy necessitated a shift towards methylprednisolone 32mg after one month. Azathioprine 50mg was associated two weeks later. Currently she is doing well with marginal AST and ALT elevation (<1.5ULN) and ANA normalisation. In the future, we will continue to treat her according to the standard of care for AIH. A 53-year-old man consulted for silent icterus since four days, seven days after completing the schedule of Pfizer-BioNTech BNT162b2 mRNA vaccination. He denied smoking, alcohol and medication use and had a negative medical history. LFTs were normal six weeks before vaccination. There was no previous SARS-CoV-2 infection. Physical examination showed jaundice. Laboratories were significant for AST (48xULN), ALT (95xULN), AP (2xULN) and GGT (12xULN). Total bilirubin was 3.1g/dL (direct 2.8mg/dL). Viral serology was negative. Ceruloplasmin and α1-antitrypsin levels were normal. Auto-immune panel showed positive ANA (1:80, speckled pattern). Total IgG was normal. Abdominal ultrasound observed steatosis. Histology was similar to the first patient. According to IAIHG criteria, pre-treatment score was 13, accounting for probable AIH. Spontaneous LFT improvement was appreciated two weeks following presentation. A 39-year-old woman was referred for LFT alterations four weeks after her first dose of Pfizer-BioNTech BNT162b2 mRNA vaccination. She had a medical history of Hashimoto's thyroiditis and rheumatoid arthritis. LFTs were normal seven months before vaccination. She reported alcohol (5 units/week) and tobacco consumption (12 cigarettes/day). No over the counter drugs were reported. There was no documented previous SARS-CoV-2 infection. Physical examination was unremarkable. Laboratories were significant for AST (11x ULN), ALT (17x ULN), and GGT (1.2x ULN). Viral serology was negative. Ceruloplasmin and α1-antitrypsin levels were normal. The auto-immune panel was negative. Total IgG was normal. Abdominal ultrasound showed mild steatosis. Histology disclosed interface hepatitis and predominant lymphocyte infiltration without biliary changes. According to IAIHG criteria, pre-treatment score was 16, accounting for definite AIH. Immunosuppressive therapy with methylprednisolone (32mg) and azathioprine (100mg) was initiated after work up, about eight weeks after documentation of LFT alteration. At that time there was a continued increase of LFT alterations with a bilirubinaemia of almost 4.0g/dL. An adequate response was observed. With her treatment of methylprednisolone 8mg and azathioprine 100mg, LFTs almost completely normalised. Above, we described the onset of AIH after vaccination with different mRNA SARS-CoV-2 vaccines in three patients. It is accepted AIH can be triggered by a plethora of viruses and drugs. Additionally, past reports have attributed development of AIH to prior vaccination suggesting a potential role of both virus and vaccine in revealing AIH in predisposed individuals. So far there is no pathophysiological link between SARS-CoV-2 vaccines and AIH. One hypothesis is molecular mimicry. In vitro data demonstrates spike protein S1 antibodies (for which the mRNA codes) have high affinity against transglutaminase 3, transglutaminase 2, anti-extractable nuclear antigen, nuclear antigen and myelin basic protein. So far, only a handful of similar cases are reported in literature. Important questions are raised concerning the safety of booster vaccination.

- Y06 -

USP53 GENE: THE NEW KID ON THE BLOCK CAUSING LOW GGT CHOLESTASIS. A. Ravindranath (1), R. Wadhwa (2), M. Wadhwa (3) / [1] Apollo BGS Hospital, Mysore, India, Pediatric Gastroenterology, [2] Apollo BGS Hospital, Mysore, India, Gastroenterology, [3] Accura diagnostics, Mysore, India, Pathology. Department

Case Report: A 14-year-old boy presented with history of pruritus since infancy for which he was being treated with topical medications at home. He also had history of recurrent wheeze for which he was receiving regular nebulisations and inhalational steroids. He developed jaundice with high colored urine for 2 months with worsening of pruritus. On preliminary evaluation his liver functions showed Total bilirubin: 18mg/dL, direct bilirubin: 12mg/dL, aspartate amino transferase: 248IU/L, alanine amino transferase: 467IU/L, total protein: 6.7g/dL, albumin: 3.8g/dL, alkaline phosphatase: 562IU/L, gamma glutamyl transpeptidase (GGT): 28IU/L. His prothrombin time and hemogram were normal. Anti HAV IgM, Anti-HEV IgM, Anti HBc IgM were negative. There was no history of intake of hepatotoxic medications. Serum bile acid level was 127mg/dL. Ultrasonogram of the abdomen showed coarse liver echoes, normal portal vein diameter and no ascites or splenomegaly. Esophagogastroduodenoscopy did not show any varices. He was born of second-degree consanguineous marriage. His father had history of pruritus and jaundice from adolescence. He developed decompensated liver disease at the age 32 years and died. Etiological work-up of father's liver disease was not available. Mother and two brothers are asymptomatic. Since he had low GGT cholestasis initial possibilities kept were progressive familial intra-hepatic cholestasis and bile acid synthetic defects. Since serum bile acid level was high bile acid synthetic defect was less likely. Liver biopsy showed bland cholestasis with mild periportal fibrosis. To confirm the etiology, exome sequencing was performed. The sequences obtained were aligned to human reference genome (GRCh38.p13) using Sentieon aligner and analyzed using Sentieon for removing duplicates, recalibration and re-alignment of indels. Sentieon haplotype caller was used to identify variants. A homozygous single base pair insertion in exon 10 of the USP53 gene (chr4:g.119268407_119268408insG; Depth: 111x) that results in a frameshift and premature truncation of the protein 5 amino acids downstream to codon 427 (p.Lys427GlufsTer5; ENST00000450251.5) was detected. On performing Sanger's sequencing in the mother, she was found to be heterozygous. The child was started on ursodeoxycholic acid and rifampicin sequentially. After 2 months of treatment pruritus subsided completely, liver functions improved. At 6 months of treatment, liver functions normalised. At a follow-up of 1 year child has gained weight of 3 kilogram and remained asymptomatic.
Discussion: Ubiquitin-specific peptidase 53 (USP53) is one of the recent genes described to be mutated in children with low GGT cholestasis. Although the exact function of USP53 is not known it is postulated that it interacts with Tight junction proteins 1 and 2 and regulates protein turnover by modulating deubiquitination. Mutated USP53 gene can affect tight junction scaffolding. Hence, USP53 mutated cholestasis has many overlapping features with that of TJP defect including wheezing and hearing loss. Since USP53 related cholestasis is only a recent addition to the set of low GGT cholestasis, long term outcomes are not definitely known. Many previously described reports have shown that the cholestasis is mild and self-limiting. In the given case, the child has been predominantly symptomatic with pruritus since infancy and visible jaundice appeared in adolescence. He has wheeze; hearing and speech are normal. Since

there is second degree consanguinity between parents, mother is heterozygous for USP53 gene mutation and father had cholestatic liver disease with decompensation it is possible that father was homozygous for USP53 gene mutation. It can be derived from the father's case that if untreated USP53 mutation related cholestasis can result in progressive liver disease in adulthood. The normalization of liver enzymes in the index case also showcases that ursodeoxycholic acid and rifampicin can reverse cholestasis reliably.

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BIRD Belgian Inflammatory Bowel Disease Research and Development

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BeSPGHAN

VVKVM Vlaamse Vereniging voor Klinische Voeding en Metabolisme

BHμSG Belgian Helicobacter and Microbiota Study Group

BSP Belgian Society of Pathology
Working group of Digestive Pathology

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