ABSTRACTS

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INDEX

BELGIAN ASSOCIATION FOR THE STUDY OF THE LIVER (BASL) /
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- A01 -

IMPACT OF PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR AGONISTS ON MYOSTEA-TOSIS IN THE CONTEXT OF METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE. N. Boliaki (1), G. Henin (2), N. Lanthier (2) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'Hépato-Gastro-Entérologie, [2] Université catholique de Louvain (UCLouvain), Belgium, Laboratory of Hepato-Gastroenterology, Institut de Recherche Expérimentale et Clinique.

Introduction: A growing body of evidence suggests that metabolic dysfunction-associated steatotic liver disease (MASLD) could be associated with fatty infiltration of skeletal muscles, known as myosteatosis. Myosteatosis is implicated in the development of insulin resistance by altering the insulin signalling pathway, could affect muscle function and possibly contributes to the severity of liver damage. A combination of peroxisome proliferator-activated receptor (PPAR) agonists is currently being evaluated as a promising treatment for metabolic dysfunction-associated steatohepatitis (MASH), the inflammatory stage of MASLD. However, the effect of pan-PPAR agonists on myosteatosis remains to be determined.
Aim: The aim of this systematic review is to evaluate the effect of PPAR agonists and their combination on myosteatosis in the context of MASLD.
Methods: We searched for combination of terms including NAFLD, MAFLD, NASH, PPAR agonist, muscle fat and intramyocellular lipids published until March 2023 using PubMed and EMBASE. Only original articles have been retained. Articles were carefully selected and examined in order to identify relevant results that align with our research topic.
Results: Our search yielded 34 results. After reading the titles and removing duplicates, 24 articles were evaluated according to our inclusion criteria. Eleven original manuscript articles were retained to answer our research question. The impact of the PPARα agonist on myosteatosis was assessed by triglyceride extraction in two preclinical studies in rats on a high-fat diet (HFD) and in insulin-resistant mice, and by proton magnetic resonance spectroscopy (MRS) in a clinical study in healthy and insulin-resistant elderly subjects. In rats fed a HFD, a two-week treatment significantly reduced quadriceps muscle triglyceride levels (-34%), as well as liver triglyceride levels (-54%), compared with controls. In insulin-resistant rats, it reduced quadriceps muscle (-44%) and liver (-40%) triglyceride levels compared to untreated rats. In a clinical study, a 60-day course of the PPARα agonist fenofibrate had no significant impact on soleus intramyocellular lipids (IMCL) or liver fat content in either insulin-resistant subjects or the healthy elderly group. In two studies on myocytes, treatment with PPARδ agonist increased the expression of the fatty acid oxidation genes CD36 and CPT1b. PPARγ agonists have been the subject of two preclinical studies and one clinical study. In the first preclinical study in Zucker diabetic fatty (ZDF) rats, treatment for one week with the PPARγ agonist rosiglitazone reduced IMCL (-40%) and hepatic steatosis (-89%) assessed by MRS and compared with the control group of ZDF rats, but had no impact on extramyocellular lipids. In a second preclinical study on ZDF rats, the PPARγ agonist pioglitazone reduced anterior tibial IMCL (-43%) assessed by proton MRS. In contrast, one year's treatment with rosiglitazone significantly increased the surface area of low density muscles (suggesting muscle fat infiltration) assessed by CT scan in patients with type 2 diabetes, while no change was observed in the placebo group. Combinations of PPAR agonists were evaluated in two preclinical studies and one clinical study. In the first preclinical study in ZDF rats on a HFD, cevoglitazar (a dual PPARα/γ agonist) significantly reduced the IMCL of the tibialis anterior, comparable to treatment with the PPARα agonist fenofibrate and the PPARγ agonist pioglitazone alone. Only fenofibrate and cevoglitazar significantly reduced hepatocellular lipids (MRS). In another preclinical study in ZDF rats, the combination of fenofibrate (PPARα) and rosiglitazone (PPARγ) did not significantly reduce gastrocnemius muscle triglyceride content (assessed by triglyceride extraction), but did with fenofibrate alone. In addition, gastrocnemius intramuscular triglyceride content was increased in ZDF rats treated with rosiglitazone alone. In contrast, in the latest clinical trial in type 2 diabetic patients, a 4-month treatment with the PPARα/γ agonist muraglitazar significantly decreased IMCL of the tibialis anterior as well as liver fat content assessed by MRS.
Conclusions: PPAR agonists, and more specifically their combination, are a promising treatment for MASH and could also have a positive impact on reducing myosteatosis. The few discrepancies noted between the studies could be explained by the different techniques used to assess myosteatosis and the possible adipogenic effect of PPARγ agonists. Further clinical research is required to fully evaluate the efficacy of these treatments on both MASH components and myosteatosis. We believe that myosteatosis should be adequately evaluated in future studies on MASLD/MASH.

- A02 -

SPATIAL PROTEO-TRANSCRIPTOMICS IDENTIFIES MACROPHAGE HETEROGENEITY IN META-BOLIC DYSFUNCTION-ASSOCIATED STEATOHEPATITIS. M. Boesch (1), A. Antoranz-Martinez (2), H. Korf (1), T. Ostyn (2), T. My Van (3), D. Newhouse (3), R. Feio-Azevedo (1), L. Van Melkebeke (1), L. Smets (1), M. Wallays (1), J. Clark (4), A. Daly (4), M. Ekstedt (5), J. Schattenberg (6), J. Boursier (7), E. Bugianesi (8), V. Ratziu (9), M. Lannoo (10),

E. Deleus (10), J. Jaekers (10), H. Topal (10), B. Topal (10), B. Boeckx (11), J. Verbeek (1), F. Bosisio (2), D. Lambrechts (11), T. Roskams (2), S. Francque (12), A. Härtlova (13), D. Tiniakos (4), Q. Anstee (4), S. van der Merwe (1), O. Govaere (2) / [1] KUL - University of Leuven, Leuven, Belgium, Laboratory of Hepatology, CHROMETA Department, [2] KUL - University of Leuven, Leuven, Belgium, Department of Imaging and Pathology, [3] NanoString Technologies, United States, NanoString Technologies, [4] Newcastle University, Newcastle Upon Tyne, United Kingdom, Translational and Clinical Research Institute, [5] Linköping University, Linköping, Sweden, Department of Health, Medicine and Caring Sciences, [6] University Hospital Mainz, Mainz, Germany, Department of Medicine, [7] Angers University Hospital, Angers, France, Hepatology Department, [8] University of Turin, Italy, Department of Medical Sciences, Division of Gastro-Hepatology, [9] sorbonne Université, France, Assistance Publique-Hôpitaux de Paris, [10] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Abdominal Surgery, [11] KUL - University of Leuven, Leuven, Belgium, Laboratory for Translational Genetics, Department of Human Genetics, [12] Antwerp University Hospital, Edegem, Belgium, Department of Gastroenterology and Hepatology, [13] University of Gothenburg, Gothenburg, Sweden, Wallenberg Centre for Molecular and Translational Medicine.

Introduction: Macrophages have been associated with the transition from normal liver to metabolic dysfunction-associated steatotic liver disease (MASLD). Yet, their dynamics and heterogeneity in the progression from isolated steatosis to metabolic dysfunction-associated steatohepatitis (MASH) remain unclear.
Aim: We aim to investigate the spatial changes in human hepatic macrophage populations during MASLD progression.
Methods: Liver biopsies from 18 MASLD-stratified patients underwent single-nucleus RNA sequencing (snRNA-seq). Spatial profiling was done by GeoMx Human Whole Transcriptome Atlas and Multiple Iterative Labelling by Antibody Neodeposition. MASH-associated GPNMB-positive (GPNMB+) macrophages were generated in vitro and challenged with lipids. Markers were explored in bulk RNA sequencing data from 206 MASLD patients and serum proteomics data from 247 patients.
Results: SnRNA-seq revealed an increase in hepatic GPNMB+ macrophages and a reduction of CD163+ Kupffer cells in MASLD. Strikingly, GPNMB+ macrophages exhibited an inflammatory profile during MASH. Key markers in bulk RNASeq data showed that GPNMB and lysozyme expression reflected MASH activity, characterised by a loss of CD163. Spatial profiling revealed that GPNMB+ macrophages were located in the portal tract and areas with active steatohepatitis. In vitro, GPNMB+ macrophages displayed a metabolic phenotype switch post lipid exposure. Furthermore, soluble GPNMB levels were elevated in patients with high MASH severity.
Conclusions: A steatohepatitis-associated macrophage subset emerged in at-risk MASH patients, distinct from portal macrophages and Kupffer cells. Furthermore, steatohepatitis-associated macrophages hold clinical relevance in MASLD grading and staging.

- A03 -

EXPLORING THE IMPACT OF DIETARY PATTERNS AND ULTRA-PROCESSED FOOD CONSUMP-TION ON THE SEVERITY OF BIOPSY-PROVEN STEATOTIC LIVER DISEASE. S. Declerck (1), G. Henin (1), S. André-Dumont (2), A. Goffaux (1), A. Loumaye (3), P. Baldin (4), P. Henry (5), P. Stärkel (2), N. Lanthier (6) / [1] Université catholique de Louvain (UCLouvain), Belgium, Laboratory of Hepato-Gastroenterology, Institut de Recherche Expérimentale et Clinique, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'Hépato-Gastro-Entérologie, [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'Endocrinologie, Diabétologie et Nutrition, [4] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'Anatomie pathologique, [5] Institut de Pathologie et de Génétique, Charleroi, Belgium, Service d'Anatomie pathologique, [6] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Service d'Hépato-Gastro-Entérologie.

Introduction: The consumption of ultra-processed foods (UPF) has significantly increased in recent years, raising concerns due to its positive association with obesity and diabetes. However, the relationship between ultra-processed foods and the severity of steatotic liver disease (SLD) has been less studied. Nonetheless, studies have indicated that both moderate (vs. low) and high (vs. low) consumption of UPF significantly elevate the risk of metabolic dysfunction-associated steatotic liver disease (MASLD). No study has been conducted on UPF consumption in alcohol-related liver disease (ALD).
Aim: Our aim is to evaluate nutritional intake and UPF consumption in SLD.
Methods: Patients with histologically confirmed hepatic steatosis (MASLD or ALD) were prospectively included, excluding those with MetALD. Anthropometric and biological data were collected. Dietary intake was assessed through a 24-hour recall, and the NOVA classification was employed to quantify ultra-processed food (UPF) consumption in grams. UPF consumption data were compared with those of the general population available in the literature (Vandevijvere et al., 2019). Finally, the severity of liver phenotype was histologically evaluated using the Beaujon score (SAF).
Results: Dietary intake and consumption of ultra-processed and processed foods were assessed in 62 SLD patients (46 with MASLD and 16 with ALD). The mean age of MASLD and ALD patients was 54 and 52 years respectively (NS). MASLD patients exhibited significantly higher mean body mass index (BMI) and abdominal circumference compared to ALD patients (35 vs. 22 kg/m², p = 0.0001; 117 vs 91 cm; p = 0.0001). Biological data showed a mean GGT level of 64

U/L in MASLD patients and 590 U/L in ALD patients (p = 0.0001), a mean HDL-C level of 43 mg/dl in MASLD patients and 89 mg/dl in ALD patients (p = 0.0001), and mean triglyceride levels of 181 mg/dl in MASLD and 196 mg/dl in ALD (NS). Both MASLD and ALD patients presented a mean moderate degree of steatosis, histologically assessed as grade 2. Among the 62 histologically evaluated patients, 3 were classified as F0 (4.9%), 12 as F1 (19.7%), 28 as F2 (45.9%), 17 as F3 (27.9%), and 1 as F4 (1.6%). One patient could not be evaluated due to the biopsy's size. Although MASLD patients had a significantly higher BMI than ALD patients, the energy intake of MASLD patients was significantly lower than that of ALD patients (1806 vs. 2716 kcal/day; p = 0.0003). In terms of nutritional intake, MASLD patients consumed more fats (73 vs. 53 g/day; p = 0.050) and fibers (17 vs. 8 g/day; p = 0.0003) than ALD patients. Our results also indicate that MASLD patients consume more ultra-processed and processed foods than the general population (ultra-processed foods: 40 vs. 35% of total energy intake (TEI); processed foods: 24 vs. 13% of TEI). When alcohol consumption is considered, ALD patients consume more processed foods than MASLD patients (2628 vs. 196 g/day; p = 0.0001). No impact of UPFs on the severity of the hepatic phenotype in terms of steatosis, inflammatory activity, and fibrosis is evident.
Conclusions: ALD patients consume more calories than MASLD patients, despite being significantly thinner. The difference in energy intake between patients with MASLD and those with ALD is mainly attributed to the caloric contribution of alcohol consumption, which is also responsible for the greater consumption of processed foods. Despite an increased consumption of UPF in MASLD patients compared to the general population, this dietary habit does not appear to significantly influence the severity of the hepatic phenotype. This observation underscores the multifactorial complexity of the disease.

- A04 -

GPR176 EXPRESSION CORRELATES WITH HEPATIC STELLATE CELL ACTIVATION IN METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE AND CHRONIC VIRAL HEPATITIS. V. De Smet (1), E. Gürbüz (1), N. Eysackers (1), A. Smout (1), P. Lefesvre (2), N. Messaoudi (3), H. Reynaert (4), I. Mannaerts (1), S. Verhulst (1), L. van Grunsven (1) / [1] Vrije Universiteit Brussel (VUB), Jette, Belgium, Liver Cell Biology Research group, [2] UZ Brussel, Brussels, Belgium, Department of Pathology, [3] UZ Brussel, Brussels, Belgium, Department of Hepatobiliary Surgery, [4] UZ Brussel, Brussels, Belgium, Liver Cell Biology Research group.

Introduction: Chronic liver disease (CLD) encompasses a range of liver disorders that can culminate in the development of fibrosis, cirrhosis, and hepatocellular carcinoma, which leads to significant global morbidity and mortality. Current therapeutic strategies for CLD target the underlying cause, but more efficient therapies are needed, especially in the context of multifactorial CLD. The activation of hepatic stellate cells (HSCs) to profibrotic, myofibroblast-like cells, plays a central role in the progression of fibrosis to cirrhosis. Since the progression of fibrosis to cirrhosis in CLD is a strong prognostic predictor, HSC activation can be regarded as a putative target for treatment of CLD. We have previously identified the orphan G-protein coupled receptor (GPCR) GPR176 as a profibrotic protein with enriched expression in mouse HSCs. Inducing hepatotoxicity in GPR176-deficient mice results in less liver fibrosis compared to their wildtype counterparts, which makes it an interesting HSC-based target for treatment of CLD.
Aim: This study investigates the correlation between GPR176 expression and human chronic liver disease.
Methods: Patient liver tissue was obtained from surgically resected specimens from the Department of Hepatobiliary Surgery of the University Hospital of Brussels (UZ Brussel). Liver cells (hepatocytes, cholangiocytes, HSC, Kupffer cells and endothelial cells) were isolated using fluorescence-activated cell sorting (FACS) and analyzed by quantitative real-time polymerase chain reaction (qPCR). HSCs for in vitro culture were isolated using a Nycodenz based method. Human HSCs were activated in vitro and analyzed using qPCR. Additionally, surgically resected specimens were subjected to tissue immunohistochemistry and immunohistofluorescence analysis. Lastly, online available transcriptome datasets of human CLD were imported from GEO and analyzed using R.
Results: Human GPR176 expression was enriched in human HSCs compared to other freshly isolated primary liver cells. In vitro cultured human HSCs exhibited increased expression of fibrogenic genes as well as GPR176 expression, confirming the association between GPR176 expression and human HSC activation. Analysis of liver transcriptome data revealed a correlation between GPR176 expression and liver fibrosis in metabolic dysfunction-associated steatotic liver disease (MASLD) and chronic viral hepatitis B and C infection. No correlation was observed with alcoholic liver disease. Finally, GPR176-positive cells were predominantly found in cirrhotic human liver tissue and co-expressed with the human HSC-marker vimentin (VIM).
Conclusions: This study establishes a correlation between GPR176 expression, human HSC activation status and human CLD. This correlation was found for MASLD and viral hepatitis B and C infection. The findings confirm GPR176 as a potential therapeutic target for liver fibrosis. Additionally, novel insight into this orphan GPCR expands our understanding of its role in physiology and pathophysiology, aiding its further de-orphanization. Further research is warranted to explore the specific mechanisms by which GPR176 influences HSC activation and its potential as a therapeutic target in CLD.

- A05 -

THE NATURAL HISTORY OF METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE WITH ADVANCED FIBROSIS. Z. Gadi (1) / [1] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology & Hepatology.

Introduction: Data on the natural history of advanced chronic liver disease (ACLD) in metabolic dysfunction-associated steatotic liver disease (MASLD) are scarce.
Aim: We aimed to describe the natural history of MASLD patients with advanced fibrosis.
Methods: We retrospectively collected patients with a biopsy proven MASLD between 2006 and November 2022 and available clinical follow-up time of at least 12 months after histological confirmation of advanced fibrosis (F3-F4). Hepatic decompensation was defined as overt ascites, overt hepatic encephalopathy (HE) or variceal bleed (VB). The development of HCC, liver transplantation and (liver-related) death was also collected.
Results: We identified 122 patients (62 F3; 60 F4), of which 6 presented with decompensation at baseline. The remaining 116 patient had a mean follow time of 5 (1-19) years. In the whole cohort 47 first decompensation events were registered in 31/122 (25%) patients distributed as Ascites/HE/VB = 22/12/13 (resp. 18/10/11%), with 11 patients experiencing more than 1 events. Excluding patients with decompensation at baseline, decompensation was seen in 25/116 (22%) patients distributed as 19/11/8 (16/9/7%), with ≥ 1 event in 8 patients. Focusing on patients with stable non-decompensating disease in the first 12 months of follow-up, thus excluding 3 patients, 32 events were noted in 22/113 (19%) with Ascites/HE/VB = 17/8/7 (15/7/6%), with ≥ 1 event in 7 patients. Decompensated patients, when compared with those without decompensation, had significantly higher (i.e. at time of diagnosis) age, spleen size, fibrosis (histology), serum potassium, serum bilirubin*, aPTT*, INR, Child Pugh Score, Na-MELD, predicted (HVPG-3P and HVPG-5P model (Reiniš, J Hep 2023) and measured Hepatic Venous Pressure Gradient (HVPG) . The platelet count, alanine transaminase*, cholinesterase*, serum sodium and steatosis (histology)* were significantly decreased. Decompensated patients were also more frequently on nonselective β-blockers (NSBB) at the time of diagnosis (11/29). Parameters with an asterisk (*) were only different in whole group analysis, including decompensation at baseline, the other only when decompensated during follow up. Interestingly, 5/29 (17.2%) patients with decompensation had F3 fibrosis and 11/28 (39%) had a HVPG ≤ 10 mmHg. HCC (4 cases) with a mean follow-up time of 211 (29-473) weeks and 23 deaths (8/23 liver-related) with a mean follow-up time 228 (55-733) weeks were noted. Of these cases 1/4 and 14/23 experienced prior decompensation.
Conclusions: In this large cohort one-fifth developed a first decompensating event with median follow-up of 4 years. Ascites was the most frequent decompensation event. Age, liver function and portal hypertension related parameters at baseline were associated with decompensation.

- A06 -

COMPARISON OF TWO METHODS FOR HEPATIC VENOUS PRESSURE GRADIENT MEASUREMENT: THE PUSH-WEDGE VERSUS BALLOON-OCCLUSION TECHNIQUE. N. Gestels (1), W. Kwanten (1), J. Derdeyn (1), T. Steinhauser (1), L. Vonghia (1), S. Francque (1), T. Vanwolleghem (1) / [1] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology and Hepatology.

Introduction: Portal hypertension (PHT) is a key determinant of morbidity and mortality in chronic liver disease. Hepatic venous pressure gradient (HVPG) measurement by hepatic vein catheterisation is currently the most validated indirect method to assess PHT. It is the strongest predictor for outcomes in compensated advanced chronic liver disease (cACLD) and an important clinical tool in the management of these patients. Two different methods exist for HVPG assessment: the balloon-occlusion technique and the push-wedge technique, but little information exist on comparability and influencing factors of both methods for assessing PHT.
Aim: We compared the results of the push wedge technique versus the occlusion balloon technique in a retrospective analysis of paired measurements, and examined possible influencing factors of discordance.
Methods: Consecutive patients, who underwent transjugular HVPG measurements between February 2018 and May 2022 at the hepatology haemodynamic lab of the University Hospital of Antwerp, were included as part of an ongoing study. Clinical, biochemical and histological data, and haemodynamic measurements were retrospectively collected. The following potentially influencing variables were included in the analysis: 1) liver histology, including fibrosis stage, disease activity and aetiology, on simultaneous transjugular biopsies; 2) parameters of liver disease severity, including MELD and Child-Pugh score; and 3) presence of intrahepatic or extrahepatic collaterals on fluoroscopy, doppler-ultrasound, CT or MRI imaging. HVPG, Wedged and Free HVP (WHVP, FHVP) with both occlusion balloon and end-hole catheter were compared. A pressure difference of >2 mmHg (hereafter referred to as disagreement) between the two methods was considered clinically relevant. A separate analysis examined the classification of patients as having PHT (HVPG > 5 mm Hg) or clinically significant PHT (CSPH, HVPG ≥ 10 mm Hg), according to the applied technique.
Results: From a total of 566 cases who underwent HVPG measurement, 149 had both types of measurement and a complete dataset for analyses; 81 (54.4%) were male, mean age was 55.4 ± 13.1 years (SD); 89 (59.2%) had advanced fibrosis (F3-F4). Most common aetiologies were alcohol-related liver disease (ALD) (30.2%) and metabolic dysfunction-associated steatotic liver disease (MASLD) (30.2%). There was presence of intrahepatic collaterals in 10.7%, and extrahepatic collaterals in 28.3% of cases. Mean HVPG was 10.83 mmHg ± 6.92 and 11.03 mmHg ± 7.04 for the occlusion-balloon and push wedge technique respectively (ns). In 36 cases (24.2%) a disagreement between techniques was observed. In the subgroup of ALD numerically more disagreement between both HVPG measurements was observed (38.2%) than in other aetiologies. The presence of intrahepatic collaterals, present in 8/36 (22.2%) of cases with disagreement, is found to be a significant influencing factor for the disagreement of HVPG measurements (Kruskal-Wallis $p<0.01$). With

increasing severity of liver disease HVPG disagreement was less frequent: 18.8% in Child-Pugh class C compared to 34.5% and 35.1% for class A and B , although not statistically significant (p = 0.218). Lastly, a gender effect was noted: HVPG was discordant in 20.6% of female versus 27.1% of male patients (p 0.04). In case of disagreement, women had more frequently higher HVPG values via the push-wedge compared to the occlusion balloon technique. The pattern of disagreement seemed to be related to aetiology: in ALD and MASLD patients push wedge HVPG was more frequently higher compared to the occlusion balloon; yet in the group with the remaining aetiologies the opposite was observed. Concerning the classification of PHT and its severity, diagnosis changed according to the applied technique in 18/149 (12.1%): 8/149 (5.3%) were discordantly classified concerning presence or absence of PHT, whereas 10/149 (6.7%) were differently classified regarding CSPH. There was, however, no clear pattern: in 10/18 discordant diagnoses the push wedge technique yielded the highest HVPG value whilst in 8/18 it was the opposite. When restricted to those with a disagreement between techniques, 8/36 cases (22.2%) were differently classified.
Conclusions: Occlusion balloon and push wedge technique yield comparable HVPG measurements in the majority of the patients. In patients with ALD and in those with intrahepatic collaterals discordance occurred more frequently.

- A07 -

HARNESSING IMMUNE DYSREGULATION IN THE SEARCH FOR SERUM BIOMARKERS FOR PRIMARY SCLEROSING CHOLANGITIS. L. Heyerick (1), K. De Muynck (1), Z. De Vos (1), S. Lefere (2), A. Geerts (2), S. Raevens (2), X. Verhelst (2), H. Van Vlierberghe (2), L. Devisscher (1) / [1] Ghent University, Ghent, Belgium, Department of Basic & Applied Medical Sciences, Gut-Liver Immunopharmacology Unit, Ghent University, Ghent, Belgium, [2] Ghent University, Ghent, Belgium, Department of Internal Medicine and Paediatrics, Hepatology Research Unit, Ghent University, Ghent, Belgium.

Introduction: Primary sclerosing cholangitis (PSC) is a progressive chronic fibroinflammatory, progressive liver disease with a high morbidity and mortality burden since no pharmacological treatments are available to slow down disease progression. Non-invasive biomarkers are required to stratify PSC subgroups at higher risk of progression to end-stage liver disease. Immune dysregulation is involved in the pathogenesis of PSC and could serve as a target in the search for new biomarkers.
Aim: To analyse cytokine and chemokine profiles in the sera of PSC patients and to determine their diagnostic and prognostic value in PSC.
Methods: Peripheral blood serum was obtained from participants with liver transplant-naïve PSC, diagnosed according to established clinical guidelines, and from age- and sex-matched healthy controls (HC). All samplings occurred in a tertiary hospital during scheduled outpatient visits. Participants had no clinical or biochemical signs of acute liver and/or gut inflammation at the time of sampling. Assessments of liver fibrosis were made based on Sirius Red staining of available liver biopsies, elastography-measurements and/or a clinical diagnosis of liver cirrhosis. Sera were analysed for a panel of candidate biomarkers, including various cytokines/chemokines and macrophage activation markers. Electronic health records were evaluated for clinically relevant variables and data were collected using REDCap. All analyses were performed using R Statistical Software (v4.2.3; R Core Team 2023).
Results: We analysed 57 patients with PSC and 15 age- and sex-matched HCs. 41 (71.9%) PSC patients had large duct disease and 35 (61.4%) had concomitant IBD. CXCL1 ($p<0.001$), IL-8 ($p<0.001$) and sCD163 ($p=0.001$) serum levels were significantly elevated in PSC patients compared with HCs, while there were no significant differences in serum levels between PSC patients with or without concomitant IBD. Surrogate biochemical markers of cholestasis and liver injury were significantly correlated with CXCL1 and with serum IL-8 concentrations. Importantly, elevated IL-8 levels were able to predict liver transplant-free survival (AUROC 0.78; 0.62-0.92 95% CI) at three years of follow-up and were associated with advanced PSC disease stage, as assessed by Mayo Risk Score and by the presence of advanced liver fibrosis (F3-4).
Conclusions: Patients with PSC have elevated concentrations of CXCL1, IL-8 and sCD163 in comparison with HCs. Moreover, in patients with PSC, serum IL-8 levels reliably identify patients that have a high risk of progression to end-stage liver disease.

- A08 -

THE NICHE MAP OF DUCTULAR REACTION-DRIVEN REGENERATION. R. Manco (1), G. Neirynck (1), I. Leclercq (1) / [1] Laboratory of Gastroenterology, Institut de Recherche Expérimentale et Clinique, Woluwe-Saint-Lambert, Belgium, GAEN.

Introduction: In chronic liver diseases, when native hepatocytes enter replicative senescence, new hepatocytes are produced via differentiation of reactive cholangiocytes, also known as ductular reaction – DR - cells. Our previous research demonstrated that during the development of chronic disease, there is a discrete but transient DR cells expansion and that the disappearance of those DR cells coincides with the appearance of new DR-derived hepatocytes. The newly

formed DR-derived hepatocytes, clonally expand to contribute to the regeneration of the liver tissue. In the injured liver, the two populations of hepatocytes, native and DR-derived, experience similar stress and DNA damage. However, the new DR-derived hepatocytes are better equipped to handle these challenges and are less likely to transform into preneoplastic nodules or HCC. Despite such a backup mechanism exists, it is not enough to fully regenerate and to avoid liver transplantation in patients. Thus, there is a need to better understand the mechanism with the perspective of discovering new targets for the implementation of new therapies to enhance in vivo DR-driven regeneration.
Aim: As all the cholangiocytes have the same capacity to respond to injury through the Hippo-YAP pathways, we propose that signals driving their differentiation into hepatocytes might reside in the local niche, such as ECM composition (i.e. Laminin) and neighbor cells (i.e. Liver sinusoidal endothelial cells - LSEC).
Methods: We used the Opn-iCreERT2; Rosa 26RYFP transgenic mouse model to be able to follow the fate of DR cells. For studying the origin of LSECs we worked with Cdh5-iCreERT2; Rosa 26RmT/mG transgenic mouse model. Chronic liver disease was simulated by injecting CCl4 3x/week for 6 weeks. Liver tissues were analyzed using immunohistochemistry, flow cytometry, and RT-qPCR techniques, and RESOLVE molecular cartography for spatial transcriptomics. Finally, single-cell sequencing was used to characterize LSECs.
Results: We have identified two populations of DR cells in the liver parenchyma: surrounded or not by laminin. Using the Molecular Cartography RESOLVE, we found that DR cells with no laminin around have a lower expression of cholangiocyte genes and an increased expression of Hnf4a suggesting a transition toward a hepatocyte-like state. Conversely, DR cells surrounded by laminin remain locked in biliary phenotype. Endothelial cells are located in close proximity to DR cells. However, the ones closer to DR with laminin around are characterized by the expression of CD34 and a higher expression of Pecam1 and Cdh5 genes, markers of capillarization. Also, during disease, the CD34+ cells have a more profibrogenic phenotype, with higher expression of the CXCR4 receptor and Timps genes.
Conclusions: Thus, CD34+ capillarized endothelial cells contribute to the maintenance of the biliary phenotype in DR cells, by preventing the degradation of the laminin that surrounds DR cells.

- A09 -

PERFORMING SPLEEN STIFFNESS MEASUREMENT IN ROUTINE CLINICAL PRACTICE: FIRST EXPERIENCES IN A MONOCENTRIC SET-UP. L. Schoenmakers (1), L. Vonghia (1), Z. Gadi (1), J. Derdeyn (1), T. Steinhauser (1), T. Vanwolleghem (1), W. Verlinden (2), S. Francque (1), W. Kwanten (1) / [1] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology and Hepatology, [2] Vitaz, Sint-Niklaas, Belgium, Gastroenterology and Hepatology.

Introduction: Non-invasive tests are increasingly used to assess several features of liver disease and to estimate the likelihood of advanced liver disease and/or clinically significant portal hypertension (CSPH). They could potentially refine and replace indications for invasive procedures such as Hepatic Venous Pressure Gradient (HVPG) measurement and liver biopsy. Additionally, the latter procedures are costly, require specific expertise and harbour risks of complications. Spleen stiffness measurement (SSM) has recently been introduced as a potential tool to assess portal hypertension.
Aim: The first aim was to analyse the feasibility and reasons for technical failure of SSM with a dedicated probe in patients scheduled for transjugular liver vein catheterisation in a single centre. The second aim was to assess the correlation between SSM and Liver Stiffness Measurement (LSM) and the diagnostic accuracy of both to diagnose clinically significant portal hypertension (CSPH).
Methods: All patients who underwent HVPG measurement for any indication between September 2021 and October 2023 were scheduled on the same day for LSM and SSM. Both were performed by using the Fibroscan® Expert 630 device and using the appropriate probe (respectively 50Hz and 100Hz). In case of LSM, data obtained with the M-probe were preferred unless there were only successful data obtained with the XL-probe. Successful LSM was defined as ≥10 valid measurements and, in case of LSM ≥7.1 kPa, an IQR/med ≤30%. Successful SSM was defined as ≥8 valid measurements and, in case of SSM ≥10 kPa, an IQR/med ≤30%. CSPH was defined as an HVPG ≥10mmHg. Data were prospectively collected and retrospectively analysed. Diagnostic performance was assessed by using the area under the receiver operating characteristic curve (AUROC). Regression analyses were performed for the HVPG (linear) and CSPH (logistic) values.
Results: Out of the 245 patient who underwent HVPG measurement, 195 patients (61.5% male, mean age 57 ± 12.24 (SD)) underwent contemporaneous LSM and SSM measurements and were included in the analysis. Main underlying aetiologies were alcohol-related liver disease (ALD) (31.8%) and Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) (20.5%). The combination of ALD and MASLD constituted 10.8% of cases. The rates of successful LSM, SSM and HVPG were 63.6%, 57.9% and 95.9% respectively. The main reason for failure of LSM and/or SSM was the presence of ascites (respectively 24.1% and 15.8%). Other reasons of unsuccessful SSM were 'unreliable results' (24), 'spleen not accessible' (too deep/high) (7), 'spleen too small' (3), 'splenectomy' (3), or 'unknown' (13). Both LSM and SSM significantly correlated with HVPG ($r = .740$ ($p < 0.001$) and $r = .362$ ($p < 0.001$) respectively), as well as with each other ($r = .295$ ($p = 0.006$)). CSPH was diagnosed in 63/121 patients who had a valid LSM value and in 75/109 patients who had a valid SSM value. Both LSM and SSM showed good performance for the diagnosis of CSPH (AUROC 0.894 and 0.716, respectively). Corresponding 90% sensitivity cutoff (rule in) values were 20 kPa for LSM and 35 kPa for

SSM whereas 90% specificity cutoffs (rule out) were 5.3 kPa and 19 kPa for LSM and SSM respectively. These cutoffs correspond with a NPV 100% and a PPV of 76.7% to rule out or in CSPH respectively for LSM, and a NPV 100% and a PPV 77.5% to rule out or in CSPH by SSM. Linear regression with two independent predictors (LSM and SSM) for the HVPG value as continuous dependent variable resulted in an adjusted R square of .587, with both significant coefficients for SSM ($p = 0.008$) and LSM ($p < 0.001$). For the diagnosis of CSPH, however, SSM was no longer significant ($p = 0.053$) in a combined model with LSM, which was significant at $p < 0.001$, with 81% of cases correctly predicted.
Conclusions: Technical success rate for SSM in this cohort of patients scheduled for HVPG measurement was nearly 60%, with failure mainly caused by ascites or volume/anatomical position of the spleen. LSM (strong) and SSM (moderate) correlated significantly with HVPG. with both being independent predictors of HVPG. For the diagnosis of CSPH both performed well but SSM was no longer a significant independent predictor when combined with LSM.

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HEPATITIS B SEROPREVALENCE IN BELGIUM ANNO 2020. A. Furquim d'Almeida (1), E. Ho (2), C. Schüttler (3), P. Beutels (4), P. Van Damme (5), N. Hens (4), H. Theeten (5), T. Vanwolleghem (1) / [1] University of Antwerp, Antwerp, Belgium, Viral Hepatitis Research group, Laboratory of Experimental Medicine and Pediatrics, [2] Antwerp University Hospital, Edegem, Belgium, Department of Gastroenterology and Hepatology, [3] Justus Liebig University, Giessen, Germany, Institute of Medical Virology, National Reference Center for Hepatitis B Viruses and Hepatitis D Viruses, German Center for Infection Research, [4] University of Antwerp, Antwerp, Belgium, Centre for Health Economics Research and Modelling of Infectious Diseases (CHERMID), Vaccine & Infectious Disease Institute (VAXINFECTIO), [5] University of Antwerp, Antwerp, Belgium, Centre for the Evaluation of Vaccination, Vaccine and Infectious Disease Institute (VAXINFECTIO).

Introduction: Hepatitis B virus (HBV) infection remains a major global public health problem, leading to approximately 820 000 deaths worldwide annually. In 2016 the World Health Organisation (WHO) launched its viral hepatitis elimination goals to decrease the HBV incidence by 90% by 2030. Population-based screening studies are of pivotal importance to assess each country's progress towards the elimination of chronic viral hepatitis as set by the WHO. HBV prevalence estimates for Belgium date from 1993/1994 and 2003, cover only Flanders and pointed to a hepatitis B surface antigen (HBsAg) prevalence rate of 0.7% and 0.66% respectively. Since 1999 the systematic vaccination of infants and 12-year-olds has been implemented in Belgium. Crucial for correct data on national HBV seroprevalence are both sensitive and specific serological assays. Automated HBsAg assays are, however, typically designed to be oversensitive and might result in an overestimation of the HBV prevalence. HBV seroprevalence studies applying HBsAg and hepatitis B core antibodies (anti-HBc) double positivity as criterium for HBV infection could potentially yield better estimates. Taken together, updated, nationwide data to evaluate Belgium's public health response towards HBV are urgently required.
Aim: We examined the Belgian HBV seroprevalence in adults anno 2020. Furthermore, we investigate the differences in HBV seroprevalence estimates applying either HBsAg seropositivity or double anti-HBc and HBsAg positivity as criterium to be regarded as HBV infected. Finally, we assessed the proportion of samples with measurable anti-HBs antibodies, as an estimate of HBV vaccine uptake.
Methods: In this prospective cross-sectional nationwide study, we evaluated the Belgian hepatitis B seroprevalence using residual serum samples that were collected during 3 collection periods in 2020 (8 – 13 June, 29 – 4 July and 7 – 12 September) at 10 private diagnostic laboratories. The number of samples in each laboratory was stratified per region, age group (10-year age bands) and sex. Samples from hospitals and triage centres were excluded. In total 3840 individual serum samples, originating from adult ambulatory patients, were analysed for HBsAg, hepatitis B surface antibodies (anti-HBs) and anti-HBc on automated analysers (Abbott Alinity I®). For HBsAg positive anti-HBc negative samples, anti-HBc confirmatory assays were performed at the Institute for Medical Virology, Justus Liebig University Giessen, Germany.
Results: A total of 3840 residual serum samples were tested and HBsAg was detected in 27 samples (signal/cut-off ratio >1), resulting in a HBsAg seroprevalence of 0.71% (95% CI 0.44% – 0.97%). However, 15/27 HBsAg positive samples were anti-HBc negative and thus serodiscordant. Independent neutralization assays revealed that all 15 serodiscordant samples were truly anti-HBc negative, thereby confirming a significant HBsAg false positivity rate for HBV infections of 55.6% on routine analysers. After confirmatory testing, an HBV seroprevalence, based on HBsAg and anti-HBc double positivity, of 0.31% (95% CI 0.14% – 0.49%) was retained. Most cases (10/12 or 83.3%) were more than 50 years old. 164/3840 samples (4.3%) were anti-HBc positive, indicative for a past HBV exposure. 41.4% (1590/3840) of the samples were HBsAg and anti-HBc double negative and had a quantifiable anti-HBs titre (limit of quantification = 2 IU/mL), suggesting prior HBV vaccination. Of those, 1116 (70.2%) had an anti-HBs titre >10 IU/mL, fulfilling criteria for a protective vaccine response. Interestingly, 74.2% (765/1031) of those who were <=12 years old in 1999 or those born in or after that year, had a quantifiable anti-HBs titre, which is in line with the Belgian vaccination policy implemented in 1999.
Conclusions: This population-based nationwide seroprevalence study estimates an HBV prevalence, based on HBsAg and anti-HBc double positivity, of 0.31% (95% CI 0.14% – 0.49%) in the sample group. Our results also illustrate that HBV prevalences based on HBsAg positivity alone overestimate the number of infections due to the frequent false

positivity of automated HBsAg assays. In low-endemic countries like Belgium, we therefore advocate confirmatory anti-HBc testing to estimate the HBV prevalence. In addition, we here show that 74.2% of those who were <=12 years old in 1999 or those born in or after that year had a quantifiable anti-HBs titre, indicative for a good uptake of the national HBV vaccination strategy.

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INSUFFICIENT IMPLEMENTATION OF PRETHERAPEUTIC HEPATITIS B AND C SCREENING GUIDELINES IN ONE NON-ACADEMIC BELGIAN HOSPITAL: THE CHOICE TRIAL (CHRONIC HEPATITIS B/C SCREENING IN PATIENTS ON IMMUNOSUPPRESSIVE THERAPY AND CHEMO-THERAPY). M. Coessens (1), W. Verlinden (1), J. Schouten (1) / [1] Vitaz, Sint-Niklaas, Belgium, Gastroenterology and Hepatology.

Introduction: Due to the increasing use of cytotoxic, immunomodulating and immunosuppressive therapy regimens, hepatitis B and C virus (HBV, HCV) reactivations are an emerging problem. Some patients develop a fulminant hepatitis or are prone to dose reduction or discontinuation of treatment. Despite effective preventive guidelines, HBV reactivation still occurs in daily practice. A survey of our research group showed that one third of participants had already witnessed a HBV reactivation in their own clinical practice, confirming poor implementation of screening guidelines. Belgian data on this topic are urgently needed to refocus where necessary.
Aim: Assessing implementation of pretherapeutic HBV and HCV screening guidelines in haematologists, oncologists, inflammatory bowel disease (IBD) specialists, rheumatologists, and dermatologists. In addition, associations between suboptimal screening practices and several factors are studied.
Methods: A retrospective study was conducted at the haematology, oncology, IBD, rheumatology, and dermatology departments of a non-academic hospital in East-Flanders, Belgium (Vitaz), from March to August 2023. All newly diagnosed patients in need of any systemic chemotherapy, immunomodulating or immunosuppressive therapy regimen with at least two documented administrations from 2009 onwards, were included. Patients with primary liver and bile duct cancer were excluded, as were patients who received investigational chemotherapy as part of a clinical trial. A correct HBV/HCV screening was defined as an HBsAg, anti-HBc and anti-HBs test/anti-HCV test ordered prior to the first therapy administration to two months after the first therapy administration. In addition, patient age, sex, nationality, subdiscipline (oncology), and the class of drugs with the highest risk of reactivation, were documented. Correlations between these variables and screening rates were assessed by means of chi-square test in SPSS version 29. At the haematology and oncology department, screening rates were evaluated before and after a hepatitis B reactivation awareness session.
Results: In total, pretherapeutic HBV and HCV screening rates were assessed for 704 patients. Initially, screening rates were analysed in 492 patients (65 haematology, 183 oncology, 132 inflammatory bowel disease, 75 rheumatology, and 37 dermatology patients, mean age 58.2 years old, M/F ratio 0.89 and 95.5% Belgians). Oncology patients were further divided into medical (135), digestive (24) and thoracic oncology (24). Haematologists predominantly prescribed high dose steroids [46.15%, high reactivation risk (HR)] and B-cell depleting agents (35.38%, HR), whereas oncologists mainly prescribed systemic chemotherapy [54.1%, moderate risk (MR)], anthracyclines (17.49%, HR), protein kinase inhibitors [19.13%, low risk (LR)] and immune checkpoint inhibitors (8.2%, MR-HR). IBD specialists most often use TNFα-inhibitors (68.94%, HR), azathioprine (21.21%, LR), and vedolizumab (8.33%, MR). Rheumatologists predominantly prescribed methotrexate (69.33%, LR) and TNFα-inhibitors (26.67%, HR). For dermatologists, these are methotrexate (54,05%, LR), TNFα-inhibitors (18.92%, HR), IL-17 and IL-23-inhibitors (10.81% and 8.11%, MR), and cyclosporine (8.11%, MR). Rates of incorrectly screened patients are high (haematology 50.77%; oncology 74.3%; inflammatory bowel diseases 38.6%; rheumatology 78.7%; dermatology 94.6%). Only 49.23% of haematological patients was correctly screened for hepatitis C virus infection. Screening rates improved in the haematology and oncology departments after the awareness session [haematology 49.23% up to 58.06% ($p<0.001$), and oncology 25.7% up to 59.12%, ($p<0.001$)]. HBV screening is more often performed correctly by thoracic oncologists than by medical and digestive oncologists ($p<0.001$). There are significant differences in screening behaviour between IBD specialists of the same department ($p=0.033$). Oncology and rheumatology patients in their 30s or 40s are screened more often ($p=0.023$, $p<0.001$). There is a trend towards suboptimal screening in patients on anthracyclines ($p=0.066$). In total, 21 patients had a HBV serology compatible with a past infection. Two of them were on a therapy with high reactivation risk (rituximab). One patient with isolated anti-HBc antibodies seroconverted (HBsAg+) and was successfully treated for hepatitis B reactivation with tenofovir. In the other patient on rituximab, hepatitis B prophylaxis was initiated. Only one patient had a positive HCV serology compatible with a spontaneous clearance.
Conclusions: Pretherapeutic hepatitis B screening is performed suboptimal in haematology and inflammatory bowel disease patients and poorly in oncology, rheumatology and dermatology patients. Suboptimal HBV screening prior to administration of anthracyclines is even more worrisome, as there is solid evidence for the high reactivation risk of this drug class. Correct pretherapeutic screening is feasible and effectively prevents the morbidity and mortality associated with hepatitis B reactivation.

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SYNERGISTIC LIGAND COMBINATIONS OF PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR ALPHA AND ESTROGEN-RELATED RECEPTOR ALPHA AMELIORATE MASLD. M. Antwi (1), S. Lefere (2), L. Koorneef (1), A. Heldens (2), K. Decroix (1), L. Onghena (2), J. Thommis (1), A. Geerts (2), L. Devisscher (3), K. De Bosscher (1) / [1] Ghent University, Ghent, Belgium, Department of Biomolecular Medicine, [2] Ghent University, Ghent, Belgium, Department Internal Medicine and Pediatrics, [3] Ghent University, Ghent, Belgium, Department for Basic and Applied Medical Sciences.

Introduction: Significant changes in human lifestyle have occurred in the past century, leading to a substantial increase in obesity. This has led to the rapidly increasing prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD), formerly known as non-alcoholic fatty liver disease (NAFLD), affecting approximately 30% of the world population. MASLD currently has no approved pharmacotherapy. Left untreated, MASLD can progress to metabolic dysfunction-associated steatohepatitis (MASH), cirrhosis and primary liver cancer. Literature findings support a close functional interconnection between the nuclear receptors (NR) peroxisome proliferator-activated receptor alpha (PPARα) and estrogen-related receptor (ERRα). Furthermore, in the De Bosscher lab, a physical interaction was uncovered between the two NRs, suggesting the presence of direct crosstalk mechanisms. Targeting both NR in tandem has not yet been investigated, which may be more appropriate and effective than monotherapy in MASLD progression.
Aim: To evaluate whether and how pharmacological modulation of (PPARα) and (ERRα) in tandem may interfere with MASLD progression.
Methods: To evaluate NR crosstalk in vitro, human hepatoma (HEPG2) cells were stimulated with palmitic acid and oleic acid (2:1 ratio) to introduce lipids-induced stress in the cells, followed by treatments with the PPARα agonist Pemafibrate (5μM) and/or the ERRα inverse agonist compound C29 (5μM). Lipid accumulation was evaluated via oil red O (ORO) staining, and its impact was monitored via qPCR. To assess NR crosstalk PPARα-ERRα in vivo, we used two MASLD mice models, a short-term and a long-term, which were fed a Western diet + fructose water. In the short-term model, 8-week-old male C57Bl/6J mice were fed for two weeks. After one week, they were administered the PPARα agonist Pemafibrate and/or ERRα inverse agonist C29 via daily oral gavage for seven days. Liver samples were collected and subjected to histological evaluation, qPCR, and RNA sequencing. In the long-term MASLD model, male mice were fed for 16 weeks, and daily oral gavage was administered for 6 weeks (week 10 to week 16). Part of the liver was perfused and fixed for scanning electron microscopy, while the rest was sampled for morphological/histological and qPCR. Differences between groups were compared using a one-way ANOVA with post-hoc testing.
Results: In the NR ligand combination of Pemafibrate and C29, we saw a trend in the reduction of lipids in HEPG2 cells compared to the single ligand treatments. In vivo, in the short-term MASLD mice model, quantitative image analysis showed an improvement in steatosis ($P < 0.001$). The RNA sequencing results clearly showed distinctly regulated clusters of genes. The combination treatment strongly affected pathways involving fatty acid beta-oxidation, lipid metabolism, and inflammation. This was also observed via qPCR. The livers in the long-term MASLD mice model appeared visually healthier with the ligand combination. Steatosis, ballooning, inflammation, MASLD activity score ($P < 0.0001$), fibrosis ($P<0.05$), and ORO ($P < 0.0001$) were also significantly improved. Scanning electron microscopy confirmed the significant decrease in steatosis and fibrosis with the combination treatment. Furthermore, the ligand combination improved gene expression of lipid metabolism, inflammation and fibrosis markers.
Conclusions: Our findings confirm that dual nuclear receptor targeting by increasing PPARα and diminishing ERRα activity may represent a viable novel strategy against MASLD.

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THE DOUBLE-EDGED SWORD OF BARIATRIC SURGERY: EXTENDING THE EXCLUDED LIMB CAN TRIGGER BACTERIAL TRANSLOCATION, LIVER INFLAMMATION AND DEATH. L. Onghena (1), A. Heldens (2), M. Antwi (2), L. Devisscher (3), H. Van Vlierberghe (3), S. Raevens (3), X. Verhelst (3), A. Hoorens (4), Y. Van Nieuwenhove (1), A. Geerts (2), S. Lefere (2) / [1] Ghent University Hospital, Ghent, Belgium, Department for Human Structure and Repair, Department of Gastrointestinal Surgery, [2] Ghent University Hospital, Ghent, Belgium, Liver Research Center Ghent, [3] Ghent University Hospital, Ghent, Belgium, Department of Internal Medicine and Paediatrics, Hepatology Research Unit, [4] Ghent University Hospital, Ghent, Belgium, Department of Diagnostic Sciences.

Introduction: Bariatric surgery (BS) is an effective treatment for obesity and associated comorbidities, including metabolic dysfunction-associated steatotic liver disease (MASLD). However, although rare, (sub)acute liver failure can occur following BS.
Aim: We applied several novel BS procedures in mice, including for the increasingly popular vertical sleeve plication (VSP) and one-anastomosis gastric bypass (OAGB), to examine the effects of surgery selection and biliary limb length on metabolic health, bacterial translocation, and survival.
Methods: Mice were fed a Western diet (WD) for 12 weeks, followed by surgery with continued WD feeding and sacrifice at weeks 13 and 20. Six different types of BS (vertical sleeve gastrectomy and plication, Roux-en-Y gastric

bypass (RYGB), and one-anastomosis gastric bypass (OAGB) with three different biliary limb lengths (25% = Omega1, 50% = Omega2, 75% = Omega3)) were performed and compared with sham surgery procedure. Gut decontamination with an oral antibiotic cocktail (amoxicillin, vancomycin, neomycin, and metronidazole) was performed in a subset of Omega3 mice, starting one week before surgery until the end of the experiment. Weight loss, MASLD severity, fat cell hypertrophy, glucose tolerance, intestinal remodeling, organ inflammation and bacterial translocation were evaluated by histology, biochemistry, glucose tolerance tests, gene expression analysis and bacterial culture. Liver histology from mice with different biliary limb lengths were assessed by an expert liver pathologist and compared to samples from patients managed at the Ghent University Hospital who had developed liver failure following biliopancreatic diversion or RYGB. Statistical differences between groups were assessed by one-way ANOVA with Tukey post-hoc tests.
Results: Relative weight loss differed significantly ($p < 0.0001$) amongst the groups at week 20. In RYGB, Omega1&2, significantly lowered relative visceral adipose tissue weight ($p < 0.0001$), fat cell diameter ($p < 0.0001$), ALT ($p < 0.01$), glucose intolerance and liver triglyceride content ($p < 0.01$) compared to sham surgery. Histologically, sham-operated mice had developed severe liver steatosis, moderate inflammation, and mild fibrosis after 20 weeks of WD feeding, which was attenuated by RYGB ($p < 0.05$) and by Omega1&2 (both $p < 0.01$). Bacterial translocation in the liver was observed in RYGB, Omega1&2 ($p < 0.001$). Unexpectedly, the Omega3 surgery resulted in 100% mortality after 20 days. To further dissect the cause of this event, we sacrificed mice with the varying Omega loop limb lengths one week after surgery. We observed inflammation in the terminal ileum and biliary limb in mice that underwent Omega3 compared to sham ($p < 0.05$). The number of bacterial colonies in the spleen and biliary limb were significantly higher after Omega3 ($p < 0.05$), combined with higher levels of hepatic inflammation (IL-12 protein and RNA levels) and bacterial content ($p < 0.05$), compared to sham. Liver histology in Omega3 mice was characterized by a mediovesicular steatosis, which we compared to histopathology features in humans. This entity closely resembled the typical histological picture observed in patients with end-stage liver disease after BS. Critically, oral gut decontamination significantly increased one-week-survival of Omega3 mice from 31.3% to 80.0%. Antibiotic treatment not only prevented bacterial overgrowth in biliary fluid ($p < 0.05$) and spleen ($p < 0.01$), but also significantly decreased serum ALT and AST levels ($p < 0.01$) in these mice.
Conclusions: BS procedures in mice, especially RYGB, Omega1&2 improve MASLD. Our studies show that mortality in longer biliary limb surgery is caused by bacterial overgrowth and inflammation of the gut-liver axis, which can be treated with oral gut decontamination. Our novel procedures open the field of research into the mechanisms of action of BS on hepatic and intestinal physiopathology.

- A14 -

SPLEEN STIFFNESS-BASED ALGORITHMS ARE SUPERIOR TO BAVENO VI CRITERIA TO RULE-OUT VARICES NEEDING TREATMENT IN PATIENTS WITH ADVANCED CHRONIC LIVER DISEASE.
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Introduction: The Baveno VI criteria have set the stage for non-invasive assessment of compensated advanced chronic liver disease (cACLD). The algorithm combining liver stiffness measurement (LSM, < 20kPa) and platelet count (> 150000/L), safely avoids screening endoscopy for varices needing treatment (VNT), but only identifies a relatively low number of patients.
Aim: We aimed to evaluate the value of spleen stiffness measurement (SSM) using spleen-dedicated elastography in ruling out VNT.
Methods: In this real-life multicenter retrospective derivation-validation cohort, all consecutive patients with cACLD (defined by LSM >10kPa) with available upper endoscopy, lab results, spleen diameter, LSM and SSM measured with spleen-dedicated elastography were included. VNT were defined as medium-large varices or small varices with red spots.
Results: In the derivation cohort (n=201, 11.9% VNT) SSM demonstrated excellent capability at identifying VNT (AUROC 0.88), outperforming LSM and other non-invasive scores. In comparison to Baveno VI criteria (33.8% spared endoscopies), the sequential Baveno VI plus SSM, as well as a novel 'spleen size and stiffness' model, were able to increase the number of patients avoiding endoscopy (66.2% and 71.1% respectively) without missing more than 5% of VNT. These findings were confirmed in an external validation cohort of patients with more advanced liver disease (n=176, 34.7% VNT) in which the number of spared endoscopies tripled (27.3% and 31.3% for SSM-based algorithms) compared to Baveno VI criteria (8.5%).
Conclusions: Spleen stiffness-based algorithms are superior to Baveno VI criteria in ruling out VNT in cACLD patients and double the number of patients avoiding screening endoscopy.

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SEMAGLUTIDE-LOADED LIPID NANOCAPSULES EFFECT ON METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER. I. Domingues (1), H. Yagoubi (1), W. Zhang (1), V. Marotti (1), E. K. Kambale (1), A. Beloqui (1), I. Leclercq (2) / [1] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, LDRI/ADDB, [2] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, IREC/GAEN.

Introduction: Metabolic dysfunction-associated steatotic liver (MASLD) is a highly prevalent chronic liver disease that can progress into end-stage conditions with life-threatening complications, and yet no pharmacologic therapy has not been approved. Drug delivery systems such as lipid nanocapsules (LNC) are a very versatile platform, easy to produce, and can induce the secretion of the native glucagon-like peptide 1 (GLP-1) when orally administered. GLP-1 analogs are currently being extensively studied in clinical trials in the context of MASLD. Our nanosystem provides with increased levels of GLP-1, triggered by the nanocarrier itself, and increased plasmatic absorption of the encapsulated synthetic analog (semaglutide).
Aim: Our goal was to demonstrate a better outcome and a greater impact on the metabolic syndrome associated with MASLD and on the liver disease progression with our nanosystem and compare the effect with the orally marketed version of semaglutide, Rybelsus, in suspension.
Methods: To that purpose, we studied the effect of our nanocarriers following a daily chronic treatment (gavage) of 4 weeks in a dietary model of MASLD, where the mice were fed a western diet plus fructose on the drinking water for 20 weeks. Throughout the treatment, body weight and glycemia levels were monitored. At the day of sacrifice, blood and liver tissue were collected.
Results: Regarding the effect of semaglutide-loaded lipid nanocapsules (SEMA RM LNC) on the metabolic syndrome associated with MASLD, we see a 14.21% reduction in non-fasting glycemia with the SEMA RM LNC group although no significant differences were attained when compared to the other treatment groups. Overall, the results show a positive impact of SEMA RM LNC towards the normalization of glucose homeostasis and insulin resistance. In the liver, no significant changes were observed regarding lipid accumulation (liver weight, hepatic lipid content and steatosis score). However, an improvement in markers related to inflammation was observed, with significant differences attained between our SEMA RM LNC with the diseased control group with markers related to cytokine expression (IL-6: *P=0.0247), immune cell infiltration (F4/80: *P=0.0334) and endotoxin-mediated inflammation (TLR4: ****P0.0001). We hypothesize that by acting on the metabolic syndrome associated with MASLD and improving insulin resistance we can show an improvement in MASLD, and prolonged treatment periods could help to show a more significative effect of our strategy.
Conclusions: The results show a higher impact on the metabolic syndrome associated with MASLD and reduced inflammation partially mitigating this way the progression of the disease. Although resolution of MASLD was not achieved, the oral administration of the nanosystem was more efficient at preventing the progression of the disease into more severe states when compared to the orally marketed version of semaglutide, Rybelsus, when administered as a suspension.

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PORTAL VEIN RECANALIZATION IN NON-CIRRHOTIC PATIENTS WITH PORTAL VEIN OCCLUSION: FIRST RESULTS OF A VALDIG STUDY. K. Troch (1), A. Denys (2), M. Praktiknjo (3), A. Baiges (4), F. Turon (4), L. Elkrief (5), A. Plessier (6), B. Guiu (7), F. Artru (8), V. Fraitzl (3), J. Garcia-Pagan (4), O. Pol (4), M. Dioguardi Burgio (9), M. Meszaros (10), M. Barrufet (4), M. Burrel (4), M. Garcia-Criado (4), A. Soler (4), L. d'Alteroche (5), A. Marot (11), P. Deltenre (12) / [1] Clinique Saint-luc Bouge, Namur, Belgium, Gastro-Entérologie, [2] Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland, Radiodiagnostic et Radiologie Interventionnelle, [3] Universitatsklinikum Munster, Germany, Gastroenterology, [4] Hospital Clinic Barcelona, Spain, Barcelona Hepatic Hemodynamic Lab, [5] CHU de Tours, France, Hépato-Gastro-Entérologie, [6] Hopital Beaujon (AP-HP), France, Hépatologie, [7] St-Eloi University Hospital, France, Radiologie Diagnostique et Interventionnelle, [8] Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland, Hépato-Gastro-Entérologie, [9] Hopital Beaujon (AP-HP), France, Radio-diagnostic, [10] St-Eloi University Hospital, France, Hépato-Gastro-Entérologie, [11] CHU-UCL-Namur site Godinne, Yvoir, Belgium, Hépato-Gastro-Entérologie, [12] Clinique Saint-Luc Bouge, CHU UCL Namur, CUB Hôpital Erasme, Belgium, Hépato-Gastro-Entérologie.

Introduction: In non-cirrhotic patients, chronic portal vein occlusion (PVO) can be associated with gastrointestinal bleeding, portal biliopathy, intestinal ischemia or abdominal pain. Portal vein recanalization (PVR) is a technique able to treat or prevent complications related to portal hypertension by addressing PVO itself. However, data of patients who underwent PVR are scarce.
Aim: Identify factors associated with PVR failure and evaluate long-term stent patency and outcome in a large series of patients with non-cirrhotic PVO.
Methods: Retrospective study collecting health-related data of patients with chronic PVO in which placement of a stent has been attempted in 6 VALDIG centers. Extension of occlusion was assessed by portography before PVR. Central

review of imaging was performed by a single radiologist expert. A TIPS was inserted at the discretion of each center when blood flow was judged non-sufficient after PVR.
Results: 85 patients were included (55 men [65%], median age 49 years [95% CI: 45-54]). Indications for PVR were gastrointestinal bleeding (n=45, 53%), portal biliopathy (n=11, 13%), the need for reducing portal pressure before surgery (n=9, 11%), abdominal pain (n=11, 13%) and other reasons (n=9, 11%). A procoagulate state was identified in 34 patients (40%) and a local prothrombotic factor in 47 patients (55%). Occlusion involved the mesenteric vein in 55 patients (65%) and/or the splenic vein in 41 patients (50%). Regarding the intra-hepatic extension of PVO, patients were classified according to Marot classification: "type 1" with occlusion limited to the main portal vein (n=38, 45%), "type 2" with involvement of portal bifurcation and extension to segmental branches (n=29, 34%), and "type 3" with extension to distal branches (n=18, 21%). Failure of PVR occurred in 18 patients: 1 in type 1 (3%), 9 in type 2 (31%) and 7 in type 3 PVO (39%) ($p<0.001$). A complication following PVR was observed in 24 patients (28%), of which 6 (7%) were considered severe. 18 patients underwent TIPS insertion in addition to PVR because of insufficient recanalization after PVR (21%), 4 in type 1, 7 in type 2 and 7 in type 3 PVO ($p=0.048$). Anticoagulation was given to 51 patients after recanalization (64%). The median follow-up was 542 days (95% CI: 374-902). In an intention-to-treat analysis performed in all patients in which PVR was attempted, 2-year PV patency was 58% (95% CI: 47-69): 76% (95% CI: 61-91) in type 1, 51% (95% CI: 33-70) in type 2 and 29% (95% CI: 5-54) in type 3 PVO ($p=0.005$). No difference in 2-year PV patency was observed in patients who received or who did not receive anticoagulation (57% [95% CI: 45-70] vs. 66% [95% CI: 40-91], respectively, $p=0.7$). Patients who had a TIPS had a lower 2-year PV patency than those who did not have TIPS (37% [95% CI: 14-60] vs. 64% [95% CI: 52-76], respectively, $p=0.04$). 2-year PV patency differed according to the indication of PVR. Patients who had PVR for abdominal pain had the worst PV patency at 2 years (23%, 95% CI: 0-49, $p=0.024$). In Cox regression analysis, 2-year PV non-patency was independently associated with PVO type 2 (RR: 4.0, 95% CI:1.5-10.9, $p=0.006$) and type 3 (RR: 5.6, 95% CI:2.0-15.8, $p=0.001$), and with abdominal pain (RR: 3.5, 95% CI:1.5-8.5, $p=0.005$). In a per-protocol analysis performed only in patients in which PVR was feasible, 2-year PV patency was 72% (95% CI: 60-83). 2-year cumulative incidence of recurrent symptoms of portal hypertension was 33% (95% CI: 23-46), 33% (95% CI: 20-55) in type 1, 27% (95% CI: 14-51) in type 2, 42% (95% CI: 23-77) in type 3 PVO ($p=0.6$). 27 patients underwent a new PVR (32%), which was successful in 14 cases (54%). 12 patients died (14%). Death was liver-related in 2 cases (1 hemorrhagic shock secondary to hepatic artery pseudoaneurysm bleeding 2 months after PVR, 1 liver failure that occurred 4 years after PVR), non-liver-related in 8 cases and unknown in 2 cases. 2-year probability of survival was 88% (95% CI:80-97).
Conclusions: PVR is feasible in most patients with PVO if there is no extension to distal branches. 2-year PV patency following PVR is 58% and 72% in intention-to-treat and per-protocol analyses. PVO types 2 and 3 and abdominal pain as an indication for PVR are independently associated with 2-year PV non-patency.

- A17 -

MITOCHONDRIAL DYSFUNCTION CHARACTERIZES THE DELETERIOUS TRANSGENERATIONAL EFFECTS OF MATERNAL OBESITY ON MASLD IN MICE AND NON-HUMAN PRIMATES. A. Heldens (1), M. Antwi (1), L. Onghena (2), J. Norlin (3), L. Devisscher (4), X. Verhelst (1), S. Raevens (1), H. Van Vlierberghe (1), R. De Bruyne (1), A. Geerts (1), S. Lefere (1) / [1] Ghent University, Ghent, Belgium, Department of Internal Medicine and Pediatrics, [2] Ghent University, Ghent, Belgium, Department for Human Structure and Repair, [3] Novo Nordisk, Copenhagen, Denmark, Diabetes, obesity & Nash, [4] Ghent University, Ghent, Belgium, Department for Basic and Applied Medical Sciences.

Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly known as nonalcoholic fatty liver disease (NAFLD), has become the most common chronic liver disease in children and adolescents. However, compared to adult MASLD, the pathogenesis is unclear, although maternal obesity has been identified as an independent risk factor. The development of a preclinical mouse model to study the pathogenesis and identify new drug targets is therefore essential.
Aim: To evaluate the effect of transgenerational maternal obesity on MASLD severity in the offspring of mice, uncover pathophysiological mechanisms and test drug candidates.
Methods: Maternal obesity was induced by feeding female C57Bl/6J mice a western diet (WD) (high-fat, high-sucrose, high-cholesterol) from 8 to 16 weeks of age. Female mice were bred to a normal chow (NC)-fed male mice. Diet was maintained during pregnancy and lactation. To evaluate the effect of multigenerational maternal obesity, female offspring were used to produce the next generations. Feeding and breeding scheme were identical to the first generation. Male offspring were weaned onto WD. NC- and WD-fed male offspring without exposure to maternal obesity were used as control groups. The development of MASLD in the male offspring was assessed at the age of 24 days and 16 weeks. MASLD severity and metabolic alterations were evaluated through histology, serum markers, RNA sequencing, and flow cytometry analysis of hepatic macrophages. Hepatic mitochondrial oxidative phosphorylation (OXPHOS) complex abundance was analyzed using blue native polyacrylamide gel electrophoresis and in-gel activity assay. To evaluate the translational potential of our findings, the publicly available GSE220102 RNAseq dataset on maternal WD in non-human

primates was analyzed. Finally, we assessed the therapeutic efficacy of FGF-21, dose-titrated based on body weight and administered via twice daily subcutaneous injection from week 8 to week 16.
Results: 16-week-old male offspring exposed to multigenerational maternal WD exhibited significantly higher body, liver and gonadal adipose tissue weight (all $p < 0.001$). Furthermore, insulin resistance, estimated by HOMA-IR, and serum ALT levels were elevated by maternal obesity. On histology, steatosis and inflammation grade, and consequently the NAFLD activity score, increased gradually with the number of maternal generations fed a WD. Similarly on flow cytometry, maternal WD was associated with infiltration of monocytes and monocyte-derived macrophages, and depletion of Kupffer cells. Fibrosis (F1-F3) was only observed in the offspring exposed to maternal WD. RNA sequencing of mouse bulk liver tissue identified four distinct clusters, namely NC-fed controls, WD-fed offspring without maternal obesity, and offspring exposed to maternal obesity with and without the development of hepatic fibrosis. Among the top 10 GO-biological processes with significantly altered genes between the groups, four were related to mitochondrial function, specifically oxidative phosphorylation. These results could be validated on qPCR. Furthermore, increasing exposure to maternal WD was associated with a decrease of hepatic OXPHOS complex content, especially affecting complexes I, IV and V. Notably, transcriptomic analysis of non-human primate offspring fed a WD confirmed our findings, as 'oxidative phosphorylation' was one of only two KEGG pathways significantly affected by additional maternal WD feeding. To study the isolated effect of the maternal diet, MASLD severity was evaluated in offspring at weaning age (24 days). At this age, body weight ($p = 0.04$) and gonadal adipose tissue weight ($p < 0.001$) were significantly increased by maternal WD. Importantly, offspring exposed to maternal WD already exhibited steatosis and inflammation, indicating that maternal diet alone can negatively impact offspring liver health. In this model, treatment with FGF-21 significantly decreased body weight and insulin resistance, and importantly, ameliorated liver steatosis, inflammation and fibrosis.
Conclusions: Maternal obesity aggravates MASLD severity in male offspring starting from weaning age, which can be reversed by FGF-21 agonism. Similar to humans, mitochondrial dysfunction is a contributor to disease severity.

- A18 -

PHOSPHATIDYLETHANOL COMPLEMENTS URINARY AND SCALP HAIR ETHYL GLUCURONIDE IN THE DETECTION OF ALCOHOL USE IN PATIENTS WITH ALCOHOL-RELATED CIRRHOSIS. B. Vanlerberghe (1), C. Dumitrascu (2), N. Van den Eede (3), F. Nevens (1), A. van Nuijs (2), J. Verbeek (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] University of Antwerp, Antwerp, Belgium, Toxicological Centre, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Laboratory Medicine.

Introduction: Ethyl glucuronide in urine (uEtG) is a short-term alcohol use biomarker (days), while EtG in scalp hair (hEtG) reflects long-term alcohol use (months). Phosphatidylethanol (PEth) is a mid-term biomarker (weeks), which could fill the gap in the detection window between uEtG and hEtG, but its validity is barely investigated in patients with alcohol-related liver disease (ALD). In addition, the reported detection windows per biomarker are highly variable, ranging from 1 to 7 days for uEtG and 2 to 4 weeks for PEth. While the assessment of any alcohol use is important in the follow-up of patients with ALD and in the context of liver transplantation, categorization of patients depending on their level of alcohol use would allow the assessment of the contributive effect of alcohol in other liver diseases such as metabolic dysfunction-associated steatotic liver disease (MASLD; or MetALD).
Aim: We assessed the diagnostic accuracy of uEtG, PEth, and hEtG to detect different levels of alcohol use, together with their optimal detection window, in patients with ALD cirrhosis. Finally, we assessed the diagnostic accuracy of fingernail EtG (nEtG) in this population, a novel long-term alcohol use biomarker.
Methods: Patients with ALD cirrhosis were included and alcohol use in the previous three months was questioned using the Alcohol Timeline Followback Method. Patients who denied any alcohol use over the last three months with at least two positive biomarkers (uEtG, PEth, or hEtG) were excluded ($n = 6$). The 1, 2, 3, 4, 5, 6, and 7-day detection windows were assessed for uEtG (cut-off 0.121 mg/g creatinine for any alcohol use). The 1, 2, 3, 4, and 5-week detection windows were assessed for PEth (cut-off 20 ng/ml for any alcohol use and 200 ng/ml for increased alcohol use (i.e. ≥2U/d for females and ≥ 3U/d for males)). To assess alcohol intake in the last 3 months, EtG was analyzed in a proximal 3-cm hair strand (cut-off >5 pg/mg for any alcohol use and >30 pg/mg for excessive alcohol use (i.e. ≥ 5U/d for females and ≥6U/d for males)), and in fingernail (cut-off >59 pg/mg for any alcohol use). Possible confounding factors were assessed by uni- and multivariate linear regression.
Results: One hundred ten patients (mean age 60.7 years (SD 10.7); male 74.5%; Child-Pugh A 59.1%) were included. UEtG ($n = 98$) yielded the highest diagnostic accuracy for the 3-day detection window, with a sensitivity of 100%, specificity of 93.4%, positive predictive value (PPV) of 81.5%, and negative predictive value (NPV) of 100% for any alcohol use. PEth ($n = 105$) yielded the highest diagnostic accuracy for the 3-week detection window, with a sensitivity of 95.2%, specificity of 98.4%, PPV of 97.6%, and NPV of 96.9% for any alcohol use. HEtG ($n = 97$) had a sensitivity of 89.7%, specificity of 86.2%, PPV of 81.4%, and NPV of 92.6% for any alcohol use in the prior 3 months. When assessing increased alcohol use in the last 3 weeks, PEth had a sensitivity of 76.9%, specificity of 89.9%, PPV of 71.4%, and NPV of 92.2%. HEtG had a sensitivity of 100%, specificity of 79.3%, PPV of 46.9%, and NPV of 100% to detect excessive alcohol use in the last 3 months. Absolute values of uEtG (B: 0.860 (Std. 0.042) ; $p < .001$), PEth (B:1.594 (Std. 0.191); $p < .001$), and hEtG (B: 0.931 (Std. 0.097); $p < .001$) only correlated with alcohol use and not with kidney dysfunction, Child-Pugh score, and sex in multivariate analysis, nor the use of loop diuretics for uEtG and hemoglobin for PEth. Nail

EtG (n = 77) had a sensitivity of 78.9%, specificity of 97.4%, PPV of 96.8%, and NPV of 82.6% for detecting any alcohol use over the last three months.
Conclusions: In patients with ALD cirrhosis, uEtG, PEth, and hEtG have an excellent and complementary diagnostic accuracy for the detection of any alcohol use in the prior 3 days, 3 weeks, and 3 months respectively, thereby establishing the "tri-test-tri-window" assessment of alcohol use. PEth and hEtG have high negative predictive values for increased and excessive alcohol use respectively. Nail EtG can provide an alternative when scalp hair is unavailable, but needs further validation.

- A19 -

BARIATRIC SURGERY IS A MAJOR INDEPENDENT FACTOR OF DISEASE PROGRESSION IN CIRRHOTIC PATIENTS WITH ALCOHOL-RELATED LIVER DISEASE. L. Onghena (1), L. Demeulenaere (2), L. Devisscher (3), H. Van Vlierberghe (4), S. Raevens (4), X. Verhelst (4), Y. Van Nieuwenhove (1), S. Lefere (2), A. Geerts (4) / [1] Ghent University Hospital, Ghent, Belgium, Department for Human Structure and Repair, Department of Gastrointestinal Surgery, [2] Ghent University Hospital, Ghent, Belgium, Liver Research Center Ghent, [3] Ghent University Hospital, Ghent, Belgium, Department for Basic and Applied Medical Sciences, Gut-Liver Immunopharmacology unit, [4] Ghent University Hospital, Ghent, Belgium, Department of Internal Medicine and Paediatrics, Hepatology Research Unit.

Introduction: Patients with a history of bariatric surgery (BS) are susceptible to developing alcohol use disorder, potentially resulting in end-stage liver disease. We have recently published that these patients can develop severe alcohol-related liver disease (ARLD), often at a younger age and despite lower cumulative alcohol intake when compared to ALRD patients without BS. However, there is paucity of data on the evolution of cirrhotic disease.
Aim: Our aim was to describe the demographics and mortality in hospitalizations over time in patients diagnosed with alcohol-related liver disease, in relation to BS.
Methods: We included patients hospitalized between 1/1/2010 and 30/09/2023 with ARLD. Data were retrieved retrospectively from the most recent hospitalization. Statistical analysis was performed using Mann-Whitney U and Chi2 tests.
Results: 46/275 (16.7%) of cirrhotic patients admitted with ARLD had a history of bariatric surgery. Patients with a history of BS were predominantly female (76.1%), in contrast to the non-BS population (29.7%) ($p < 0.0001$) and were significantly younger at the time of diagnosis (46 vs 58 years, $p < 0.0001$), as well as the first hospitalization (48 vs 61, $p < 0.0001$). Liver disease evolved at a faster pace in BS group with a shorter time to first hospitalization (5 vs 13 months, $p = 0.036$), and a shorter time between first and second (45 vs 114 months, $p = 0.011$) and second and third (31 vs 86, $p = 0.006$) hospitalizations. Alcoholic steatohepatitis was diagnosed more frequently (41.3% vs 20.6%, $p = 0.003$), with higher bilirubin levels (7.7 vs 4.1 mg/dL, $p = 0.011$) during first hospitalization in the BS group. The population with primary hospitalization due to ACLF was significantly larger in the BS group (60.9% vs 27.6%, $p < 0.0001$) and throughout the following hospitalizations remained more prominent in the BS group; with significantly more patients hospitalized with pre-ACLF as well (8.7% vs 2.6%, $p = 0.045$). Conversely, stable decompensated cirrhosis occupied a substantial share in the group without BS during the first four ($p = 0.004$, $p < 0.0001$, $p < 00.1$, $p = 0.034$) hospitalizations. Modeled transplant-free survival, through Cox proportional regression analysis with age at diagnosis, was lower in the BS group ($p = 0.004$), with the main cause of death was ACLF in 81.3% vs 25.0% in the control group. Within the ACLF hospitalizations, alcoholic steatohepatitis (25.0% vs 12.9%, $p = 0.0014$) and bacterial infection (57.1% vs 43.5%, $p < 0.0001$) were predominant triggers for the BS group, whereas gastro-intestinal bleeding (3.6% vs 21.0%, $p = 0.037$) occurred significantly more often in the non-BS group. The weekly amount of alcohol consumed during drinking periods (41.0 (22.5, 64.5) vs 55.0 (35.0, 80.0) units/week, $p = 0.002$) and duration of use (8.0 (5.0,15.0) vs 23.0 (15.0, 30.0) years, $p < 0.001$) were significantly lower in the BS group.
Conclusions: Cirrhotic BS patients hospitalized with ARLD develop acute decompensations at a faster pace, with more overall ACLF hospitalizations, with an equally evolving cumulative mortality, despite being 12 years younger on average. There is a need for prospective research to substantiate stricter pre-BS patient selection guidelines, especially regarding alcohol use.

- A20 -

CREATION OF CRACKERS ENRICHED WITH POLYUNSATURATED FATTY ACIDS WITH BENEFITS FOR METABOLIC PARAMETERS: A DOUBLE-BLIND RANDOMISED CONTROLLED TRIAL IN OVERWEIGHT SUBJECTS. C. Dénos (1), B. Pachikian (2), S. Hdidou (1), E. Dierge (1), C. Debier (1), P. Trefois (3), Y. Larondelle (1), N. Lanthier (4) / [1] Université catholique de Louvain (UCLouvain), Belgium, Louvain Institute of Biomolecular Science and Technology, [2] Université catholique de Louvain (UCLouvain), Belgium, Center of Investigation in Clinical Nutrition (CICN), [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service de Radiologie, [4] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'Hépato-Gastro-Entérologie.

Introduction: There is a considerable increase in metabolic disorders in the world population, such as obesity, type 2 diabetes, cardiovascular disease and steatotic liver disease associated with metabolic dysfunction (SAMLD). There

is growing interest in understanding dietary lipid metabolism and improving food quality for human well-being and disease prevention. In particular, certain polyunsaturated fatty acids (PUFAs) such as alpha-linolenic acid (ALA), docosahexaenoic acid (DHA), rumenic acid (RmA) and punicic acid (PunA) are known to have positive biological activities on human health and have attracted the interest of many scientists. The supply of healthy foods is also a priority.
Aim: The aims are to study the feasibility of incorporating eggs naturally enriched with ALA, DHA, RmA and PunA into crackers, and to test their tolerance and their effects on metabolic parameters and body composition in humans fed with these test crackers compared with control crackers (Omegasnack study).
Methods: A double-blind randomized controlled trial was conducted on 25 overweight subjects with abdominal adiposity. Hens were fed with pomegranate oil and flax seeds to obtain eggs naturally enriched in ALA, DHA, RmA, PunA, which were used in the test crackers and hens were fed with olive oil to obtain eggs naturally enriched in oleic acid, which were used in control crackers. Human subjects were randomly assigned into two groups: a control group consuming control crackers and a test group receiving test crackers. Each group consumed a serving of the respective crackers (67.5 grams) as an afternoon snack every day for 70 days. Clinical, anthropometric and biological data were evaluated. Body composition was assessed by bioimpedance analysis and abdominal CT scan. Liver status was assessed by non-invasive scores and transient elastography.
Results: Fatty acids of interest were efficiently incorporated into test crackers made with eggs from hens fed modified diets. The test crackers were significantly enriched with PUFAs n-3 such as DHA and conjugated fatty acids such as PunA and RmA, providing a daily intake of 141, 662 and 1119 mg, respectively ($p<0.05$ versus control crackers). The characteristics of the subjects were as follows with no difference between the two groups: mean age of 45.9 years, mean BMI of 28.1 kg/m², mean waist circumference of 99.1 cm, median hepatic elasticity of 4.6 kPa, mean controlled attenuation parameter of 258 dB/m. Insulin resistance was noted, with a mean HOMA-IR of 2.9. The mean triglyceride level was 105.3 mg/dL and the mean fatty liver index 48.5. The median visceral fat area was 114.3 cm². The median sekeletal muscle index was 48.6 cm²/m². The estimated compliance was 95% in both groups. Test and control crackers were well tolerated and increased satiety while reducing hunger and intention to eat in the future, but no impact on weight or waist circumference was noted. There was no change in circulating cholesterol or triglyceride levels. Liver transaminases and GGT remained stable during the study for both control and test group. Glucose metabolism and insulin resistance parameters were measured in the fasted state and did not appear to be strongly affected by either type of crackers. There was no difference in body composition (liver fat, adiposity, muscle surface or density) between the two groups. A significant transient decrease in HOMA-IR was detected with the test crackers during the study (HOMA-IR 2.77 ± 1.26 vs. baseline 3.15 ± 1.27, $p< 0.05$). The fatty acid composition of plasma and red blood cells was modified by the type of cracker consumed. In the test group, RmA and PunA significantly increased in plasma (12.9 ± 8.8 vs. 4.7 ± 2.6 mg/L and 4.4 ± 2.4 vs. ND, $p < 0.05$) and RmA was efficiently incorporated into human red blood cells (0.33 ± 0.08 vs. 0.09 ± 0.03 weight % of total identified fatty acids, $p<0.05$).
Conclusions: PUFAs can be successfully incorporated into snacks without adverse effects. The study demonstrates their potential long-term benefits by effectively incorporating them into plasma and red blood cells. These findings argue in favor of studying the inclusion of PUFAs in snack products to promote health through long-term trials in specific groups of patients.

- A21 -

TELOMERE LENGTH IS SIGNIFICANTLY REDUCED IN ALCOHOL-ASSOCIATED HEPATITIS. D. Penrice (1), N. Jalan-Sakrikar (1), B. Kassmeyer (1), P. Kamath (1), V. Shah (1), D. Simonetto (1) / [1] Mayo Clinic, Rochester, United States, Gastroenterology and Hepatology.

Introduction: Telomeres are DNA-protein structures located at the end of chromosomes which prevent DNA degradation and unwanted repair. Telomeres naturally shorten with ageing; however, ineffective maintenance of telomere length has been implicated in many diseases involving organs with high regenerative capacity. Alcohol-associated hepatitis (AAH) is an acute severe form of liver disease which develops in up to 30% of heavy alcohol users and is associated with high mortality. Impaired liver regeneration is one of the hallmarks of AAH and whether telomere shortening may play a role remains unknown.
Aim: To determine whether there is an association between telomere shortening and AAH.
Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from plasma samples from 88 subjects with AAH, 64 heavy drinkers without liver disease (HD), and 59 healthy controls (HC). All subjects were enrolled in the AlcHepNet Consortium Study. Telomere length was measured in DNA isolated from PBMCs using Monochrome Multiplex Quantitative PCR (MMQPCR) and reported as telomere/single-copy gene (T/S) ratio. Liver FFPE sections were obtained from 9 subjects with AAH, 9 subjects with alcohol-associated cirrhosis (Alc Cirr), and 8 HC. Samples underwent fluorescence in situ hybridization with telomere probe (FISH). FISH intensity was calculated as measure of telomere length (~100 hepatocytes/subject) in a blinded fashion.
Results: Median PBMC T/S ratio was 1.29 (±0.13) in the HC group, 1.23 (±0.20) in the HD group, and 1.13 (±0.13) in the AAH group ($P<0.001$). The HC group was younger (mean age 35) and had a lower proportion of males (32%), however HD and AAH groups were similar (64% vs 55% males, and 48 vs 46 mean age. The HD group also consumed

more alcohol than the AAH group, 140 g/day vs 112 g/day (P<0.001) respectively. No relationship was observed between T/S ratio and lifetime alcohol use (r=0.02, p=0.85). Additionally, no relationship was noted between T/S ratio and MELD score (r=0.02, p=0.87). Median telomere intensity score (TSI) in liver tissue samples was 718 (±83) in the healthy control group, 561 (±72) in the Alc Cirr group, and 491 (±63) in the AAH group (P=0.008). The significantly decreased telomere length in the AAH group was seen despite subjects being younger than the cirrhosis group (median age 34.1 in AAH, 46.5 in Alc Cirr, and 49.8 in HC).
Conclusions: Significantly reduced telomere length was observed in PBMCs and hepatocytes of patients with AAH. These findings suggest global accelerated telomere attrition in AAH rather than an organ-specific phenomenon which may carry diagnostic, prognostic, and therapeutic implications.

- A22 -

BARIATRIC SURGERY POST-LIVER TRANSPLANTATION: A BELGIAN NATIONWIDE STUDY. L. Onghena (1), A. Geerts (2), F. Berrevoet (3), J. Pirenne (4), J. Verbeek (5), E. Bonaccorsi-Riani (6), G. Dahlqvist (7), L. Vonghia (8), O. Detry (9), J. Delwaide (10), S. Lefere (11), Y. Van Nieuwenhove (1) / [1] Ghent University Hospital, Ghent, Belgium, Department for Human Structure and Repair, Department of Gastrointestinal Surgery, [2] Ghent University Hospital, Ghent, Belgium, Department of Internal Medicine and Pediatrics, Hepatology Research Unit, [3] Ghent University Hospital, Ghent, Belgium, Department for Human Structure and Repair, Department of General and Hepatobiliary Surgery and Liver Transplantation, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department for Abdominal Transplant Surgery and Coordination, [5] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology & Hepatology, [6] Cliniques universitaires Saint-Luc, Brussels, Belgium, Abdominal Transplant Unit, [7] Cliniques universitaires Saint-Luc, Brussels, Belgium, Department of Hepatogastroenterology and Liver Transplantation, [8] Antwerp University Hospital, Edegem, Belgium, Division of Gastroenterology and Hepatology, [9] CHU Liege, Liège, Belgium, Department of Abdominal Surgery and Transplantation, [10] CHU Liege, Liège, Belgium, Department of Hepatogastroenterology, [11] Ghent University Hospital, Ghent, Belgium, Liver Research Center Ghent.

Introduction: Weight gain and metabolic dysfunction-associated steatotic liver disease (MASLD) pose a rising graft concern post-liver transplantation (LT). Bariatric surgery (BS) can be considered for post-LT weight gain, although the literature is limited and the long-term outcome still uncertain. We previously reviewed the literature and concluded that timing is crucial when considering BS in a population with liver disease or transplantation.
Aim: Our current aim was to describe the demographics, mortality, and effect of BS in a post-LT population.
Methods: We conducted a national retrospective analysis in 5 Belgian transplant centres and included 25 patients with a liver transplantation between 1/1/2000 and 31/12/2018 followed by a bariatric procedure between 1/1/2005 and 31/12/2020. 187 LT patients without BS were included for comparison. Clinical, biochemical and outcome data were retrospectively retrieved. Statistical analysis was performed using the t-test, Mann-Whitney U, and Chi2 tests.
Results: In our nation-wide sample, 25 patients had undergone BS post-LT, at a median 3.5 (2.1, 5.6) years after LT. Twenty-one (84.0%) patients received a sleeve gastrectomy (SG), 3 (12.0%) a Roux-en-Y gastric bypass (RYGB) and 1 (4.0%) a one-anastomosis gastric bypass. All but one procedure (96.0%) were performed laparoscopically. Patients were predominantly male (72.0%), with a lower age at time of transplantation compared to non-BS population (54.5 vs 60.6, $p < 0.0001$). Transient acute kidney failure (20.0%) was the only short-term complication occurring in more than one patient, all after SG. Weight loss was significant and sustained, with a decrease in BMI from 41.0 ± 4.5 pre-BS to 32.6 ± 5.8 ($p < 0.0001$) 1 to 3 years post-BS and 31.1 ± 5.8 ($p < 0.0001$) 3 to 5 years post-BS. Post-LT pre-BS three (12.0%) patients presented with recurrent and one (4.0%) de novo MASLD, with 100% resolution post-BS ($p = 0.016$). Notable reductions were observed in ALT levels (40.5 ± 28.5 U/L to 27.1 ± 25.1 U/L post-BS, $p = 0.051$) and HbA1c levels (6.9 ± 1.6 to 6.0 ± 1.4 post-BS, $p < 0.0001$). Daily mycophenolic acid intake rose from 1000.0 ± 288.7 mg/day to 1392.8 ± 1619.3 mg/day ($p < 0.0001$), while the dose of ciclosporin decreased from 258.3 ± 91.7 mg/day to 146.0 ± 107.4 mg/day ($p = 0.137$). Three patients were re-transplanted, and eight patients died, of which five (20.0%) due to a non-hepatic malignancy and one (4.0%) due to liver failure. Given the small sample size and relatively high mortality due to competing risks, a statistical analysis of patient or transplant-free survival was not feasible.
Conclusions: SG is the favored BS post-LT and has proven to be safe and feasible in a post-LT setting. SG post-LT is a valid treatment for de novo and recurrent MASLD post-LT. Although we report on the largest cohort to date, there is still a need for larger cohorts to examine the effect of BS on graft survival.

- A23 -

SPATIAL MAPPING OF THE FIBROTIC RESPONSE IN A MOUSE MODEL OF ALAGILLE SYNDROME. S. Verhulst (1), F. Hildebrandt (2), L. Sevenants (3), J. Ankarklev (2), L. van Grunsven (1), E. Andersson (3), N. Van Hul (3) / [1] Vrije Universiteit Brussel (VUB), Jette, Belgium, Liver Cell Biology Research Group, [2] Stockholm University, Stockholm, Sweden, Department of Molecular Biosciences, [3] Karolinska Institutet, Karolinska University Hospital, Sweden, Department of Cell and Molecular Biology.

Introduction: Alagille syndrome (ALGS) is a rare genetic disorder characterized by bile duct paucity, usually caused by mutations in JAG1 or, in fewer cases, NOTCH2. Despite its known genetic basis, ALGS is marked by a high degree of phenotypic variability with no clear genotype-phenotype correlation. Among affected children with cholestatic ALGS, approximately 60-75% may require liver transplantation, while others will spontaneously recover their native liver function.
Aim: Using the Jag1Ndr/Ndr mouse model recapitulating key features of ALGS, we aim to study disease progression and liver recovery, or the lack thereof, focusing on the fibrotic response and microenvironment. In parallel, we aim to characterize the heterogeneity of Jag1Ndr/Ndr phenotype presentation. Ultimately, we aim to understand why patients with severe ALGS are unable to build an appropriate regenerative response.
Methods: Plasma and livers of outbred Jag1+/+ (n=40) and Jag1Ndr/Ndr (n=47) mice were collected at postnatal day 30 (P30). Body and liver weight were measured. Plasma was analyzed for liver function (Bilirubin, Bile acids, ALP, ALT). Paraffin sections of the liver were stained for αSMA (activated hepatic stellate cell) and with sirius red (collagen deposition). Jag1Ndr/Ndr mice were assigned to bins based on phenotype severity. Spatial transcriptomics (ST) was performed on two frozen Jag1+/+liver sections; two "intermediate", and four "severe" Jag1Ndr/Ndr liver sections. ST sequencing data of an estimated 1000 spatial spots was analyzed (each spotted array is 100m in diameter, and contains mRNA captured from 10-60 cells). Cell communication analysis on ST was performed using CellChat.
Results: Strong cholestasis was observed in all Jag1Ndr/Ndr pups at birth. At P30, Jag1Ndr/Ndr mice could be categorized into three phenotypic groups based on body weight, plasma levels and absence/presence of bile infarcts in the liver : (1) a mild phenotype characterized by clear plasma and restored liver function (15 out of 47 Jag1Ndr/Ndr mice, representing patients with recovered livers), (2) an intermediate severity phenotype with fibrotic response and ongoing bile infarct (BI) resolution (21/47 mice), and (3) a regeneration-impaired or severe phenotype marked by severe jaundice, low body weight and large BIs (11/47 mice, representing patients likely to require liver transplantation). Analysis of BIs revealed distinct cellular characteristics, with the presence of activated hepatic stellate cells (αSMA+ cells) and fibrosis in Intermediate Jag1Ndr/Ndr livers. Severe cases exhibited larger BIs, often lacking αSMA+ infiltration, indicative of a defective wound-healing response. Spatial transcriptomics performed on intermediate and severe Jag1Ndr/Ndr livers, revealed elevated expression of genes associated with extracellular matrix, such as Col1a1, Col1a2, and Col5a2, in livers of intermediate Jag1Ndr/Ndr mice compared to severe mice. This high expression, specifically within the bile infarct, serves as confirmation of fibrosis development. Analysis of gene signatures related to quiescent (Rgs5, Colec11, Lrat) and activated (Lox, Col6a3, S100a6) hepatic stellate cells (HSCs) indicated that livers from wild-type and severe phenotypes predominantly contains quiescent HSCs, whereas the intermediate phenotype showed a prevalence of activated HSCs. To confirm these findings suggesting an active reparative process in intermediate phenotype and an impaired/delayed recovery in severe mice, we are in the process of analyzing ST data on an additional set of intermediate and severe livers. More in-depth analysis indicates a potential significant involvement of neutrophils in the regenerative response in ALGS. Cell communication signals that target regenerating infarcts, such as Macrophage migration inhibitory factor (MIF), Tenascin and Colony Stimulating Factor (CSF) signalling, are currently under investigation to elucidate the factors influencing liver regeneration and the variability observed across different cases.
Conclusions: Jag1Ndr/Ndr mice recapitulate a broad spectrum of liver disease in ALGS at P30. The data indicates a lack of reparative response in severe mice. The prevalence of fibrotic bile infarcts accompanied with activated hepatic stellate cells in intermediate Jag1Ndr/Ndr mouse livers contrasts with the predominantly non-fibrotic bile infarcts in severe Jag1Ndr/Ndr mice. Compromised activation of hepatic stellate cells in severe Jag1Ndr/Ndr mice could underlie the failure of adequate liver recovery. Our future focus will explore cell communication signals in and around infarcts, providing valuable insights into the underlying mechanisms of disease progression in ALGS.

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FRAILTY IN MASLD PATIENTS IS ASSOCIATED WITH THE PRESENCE OF DIABETES AND THE DEGREE OF LIVER FIBROSIS. S. Declerck (1), G. Henin (1), S. André-Dumont (2), A. Goffaux (1), G. Dahlqvist (2), A. Loumaye (3), E. Pendeville (4), T. Lejeune (4), M. Valet (5), N. Lanthier (2) / [1] Université catholique de Louvain (UCLouvain), Belgium, Laboratory of Hepato-Gastroenterology, Institut de Recherche Expérimentale et Clinique, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'Hépato-Gastro-Entérologie, [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'Endocrinologie, Diabétologie et Nutrition, [4] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service de Médecine physique et Réadaptation, [5] Université catholique de Louvain (UCLouvain), Belgium, Neuro Musculo Skeletal Lab (NMSK).

Introduction: Loss of muscle strength and mass has been identified as a predictive factor for mortality. It is now evident that the loss of muscle mass and function, or sarcopenia, plays also a significant role in the development and severity of advanced liver diseases. However, the links between muscle strength and the severity of the hepatic phenotype in earlier stages of steatotic diseases are still underexplored.
Aim: Our aim is to assess the relationships between muscle strength, frailty, and the severity of liver disease in MASLD patients.

Methods: In this prospective study, the frailty of MASLD patients was assessed using the liver frailty index (LFI), including a handgrip strength test for the dominant hand, a balance test, and the time required to perform five sit-to-stand. Forearm and quadriceps muscle strength were measured using handgrip and an isokinetic dynamometer (Cybex®). Hepatic disease severity was evaluated by transient elastography, based on the controlled attenuation parameter (CAP) and elasticity. The presence of diabetes was defined by hypoglycemic medication use. Insulin resistance was evaluated in non-diabetic patients using the HOMA-IR method.
Results: 152 patients diagnosed with MASLD were included in this study. The demographic composition of the cohort demonstrated a balanced distribution between genders, with 49% females and 51% males. The mean age was 56 years (range: 19 to 78 years), and the mean body mass index (BMI) was 33 (range 22 to 60 kg/m²). There was a high prevalence of diabetes in the cohort, affecting 45% of participants. Metabolic parameters revealed a mean controlled attenuation parameter (CAP) of 328 dB/m, indicating severe hepatic steatosis. The mean liver elasticity was 8 kPa (range: 2 to 49 kPa). Among the patients assessed by transient elastography, 54 patients were classified as F0-F1 (36.5%), 48 patients as F2 (32.4%), 31 patients as F3 (20.9%), and 15 patients as F4 (10.2%). The mean handgrip strength was 39.1 kg for males and 20.3 kg for females ($p = 0.0001$). The mean quadriceps strength was 106.9 N-m in males and 72.9 N-m in females ($p = 0.0001$). Using the LFI, 51 patients (40%) were identified as robust, 70 (56%) as pre-frail, and 5 (4%) as frail. Quadriceps muscle strength was significantly lower in frail patients compared to the robust patients (mean strength: 46.7 vs. 111.8 N-m; $p = 0.0036$). Frailty was not associated with the degree of steatosis assessed by CAP or insulin resistance measured by HOMA-IR. However, frailty was associated with age ($r = 0.4559$, $p = 0.0001$). Besides age, the presence of diabetes was associated with increased frailty (mean LFI 3.3 vs. 2.96 in non-diabetic patients, $p = 0.0122$) and also higher liver elasticity (mean LFI: 2.97 in F0-F2 vs. 3.5 in F3-F4 patients; $p = 0.0008$).
Conclusions: Frailty and decreased muscle strength are associated with the essential components of MASLD, namely the presence of type 2 diabetes and the degree of liver fibrosis. Other factors such as age and gender should also be considered. This underscores a potential liver-muscle axis in the pathogenesis of the disease.

- A25 -

CELL COMMUNICATION NETWORK IN DISEASED LIVERS REVEALS LYMPHOTOXIN BETA AS A POTENTIAL INDUCER OF HEPATIC STELLATE CELL ACTIVATION. S. Verhulst (1), V. Merens (1), A. Smout (1), L. van Grunsven (1) / [1] Vrije Universiteit Brussel (VUB), Jette, Belgium, Liver Cell Biology Research Group.

Introduction: Liver pathologies cause approximately 2 million deaths per year worldwide, including 1 million due to complications of liver cirrhosis. Common causes include hepatitis infection, excessive alcohol intake or unhealthy diets. Cirrhosis is an advanced stage of fibrosis characterized by an excessive accumulation of extracellular matrix proteins. One of the key players in this fibrotic process are hepatic stellate cells (HSCs). During any type of liver injury, HSCs start to activate into a myofibroblast phenotype which produce large amounts of ECM that results in an increased stiffness of the liver. There are currently no approved anti-fibrotic therapies available in the clinic that can cure patients with liver fibrosis.
Aim: In this study we aimed to create a comprehensive and interactive network that incorporates available scRNA seq data of healthy and diseased human and mouse livers. Using this network, we want to further unravel the signalling pathways that drive HSC activation.
Methods: To establish an intercellular communication network between diverse liver cell types, we used publicly available single-cell RNA sequencing (scRNAseq) datasets from human cirrhotic livers (GSE48452) and different diseased mouse livers, including fatty livers (GSE192742, GSE129516) and fibrotic livers (GSE171904, GSE145086). We developed a novel cell communication methodology called LiNiCom, which integrates two different communication algorithms, LIANA and multiNicheNet. We extracted all potential ligands capable of activating HSCs using LiNiCom and validated these through in vitro experiments, using 2D monolayer cultures of primary mouse HSCs and primary multicellular mouse liver spheroids containing HSCs, liver sinusoidal endothelial cells, Kupffer cells, and hepatocytes. Evaluation of HSC activation was performed by real-time PCR.
Results: To create a comprehensive cell communication network in diseased livers, we developed a novel cell communication tool that combined LIANA, an algorithm designed to predict cell communication by looking at the expression of ligands and receptors, and NicheNet, an algorithm that identifies ligands based on downstream transcription effects. This integrated approach overcomes limitations associated with threshold-based strategies in NicheNet. Using this integrative cellular communication network tool, we identified ligands capable of promoting HSC activation; 39 ligands in cirrhotic human livers and 49 in diseased mouse livers, with an overlap of 12 ligands in both species. Overlapping ligands include the well-known activators such as TGFβ, TNFα, and LGALS3, alongside less known ligands, including lymphotoxin beta (LTB), calreticulin, and lumican. None of these newer ligands were able activate mHSCs in 2D cultures, however, LTB activated HSCs in primary liver spheroid cultures by increasing the gene expression of HSC activation markers Acta2, Lox, Col1a1 and Col3a1.
Conclusions: We combined the LIANA and NicheNet algorithms into a novel cell communication network tool LiNiCom, which identifies active ligand-receptor interactions in diverse cell types. Using LiNiCom we successfully generated a cell communication network between all cell types in diseased livers and revealed potential ligands that promote HSC

activation, including LTB, that can effectively activate HSCs in primary liver spheroid cultures. While in vivo validation is required to further establish the role of LTB in chronic liver disease, we believe that LTB can be a new target for the development of anti-fibrotic therapies. Furthermore, LiNiCom can be applied to non-liver scRNAseq data sets and will be available soon.

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THE ROLE OF IRON-CATALYZED FERROPTOTIC CELL DEATH IN AN EXPERIMENTAL MODEL OF METABOLIC DYSFUNCTION-ASSOCIATED STEATOHEPATITIS. C. Peleman (1) / [1] University of Antwerp, Antwerp, Belgium, Medicine and Health Sciences.

Introduction: Hepatocyte cell death is a hallmark of metabolic dysfunction-associated steatohepatitis (MASH), but the dominant subtype of hepatocyte cell death remains to be elucidated. Accumulating evidence points towards ferroptosis as an important driver in MASH pathogenesis. Ferroptosis is a type of regulated necrotic cell death executed by iron-catalysed peroxidation of polyunsaturated fatty acids (PUFA) in membrane phospholipids. Because no approved pharmacotherapy is currently available, therapeutic targeting of cell death mediated injury may constitute a novel treatment option for this highly prevalent liver disease.
Aim: We examined the determinants of increased ferroptosis sensitivity of hepatocytes in vitro and the effects of ferroptosis inhibition on MASH in vivo in a murine dietary model.
Methods: In vitro, we studied the sensitivity of HepG2 cell line to undergo ferroptosis after exposure to a MASH environment, i.e., the application of oleic and palmitic acid (both non-PUFA), glucose, insulin and cytokines. The percentage of cell death after ferroptosis inducer ML162 was measured using the Sytox Green assay. Lipidomics analysed the membrane phospholipid composition of HepG2 cells to elucidate determinants of ferroptosis sensitivity. In vivo, in C57BL/6J mice fed the choline-deficient L-amino acid defined high-fat diet (CDAHFD) for 4 weeks, the ferroptosis markers malondialdehyde (MDA) and 4-hydroxynonenal (4HNE) were assessed. The effect of ferroptosis inhibition by the third-generation ferrostatin analogue UAMC-3203, both in preventive and curative setup, was tested in mice fed the CDAHFD or standard diet (SD) on serum liver enzymes, liver volume, liver fat content and histology.
Results: In vitro, steatotic HepG2 cells displayed higher sensitivity towards ferroptosis inducer ML162, as evidenced by lower EC50 values for cell death with Sytox Green assay. Mechanistically, excess non-PUFA fatty acids increased incorporation of PUFA in membrane phosphatidylglycerol in HepG2 cells, rendering them more vulnerable towards ferroptosis. In vivo, when fed CDAHFD murine livers displayed MASH with increased hepatic MDA levels and panlobularly increased 4HNE staining on immunohistochemistry, compared to controls displaying normal liver histology. Simultaneous (preventive) treatment with UAMC-3203 for 4 weeks reduced hepatic MDA ($p < 0.01$ treatment effect), liver volume ($p < 0.001$) and alanine transaminase levels ($p < 0.01$) in CDAHFD, compared to vehicle treatment. Likewise, the therapeutic administration of UAMC-3203 during the last 2 out of 4 weeks of diet reduced MDA ($p < 0.05$) and alanine transaminase levels ($p < 0.01$), while attenuating macrovesicular steatosis compared to vehicle.
Conclusions: In summary, non-PUFA supplementation to hepatocytes in vitro caused an unexpected increase in ferroptosis sensitivity. Ferroptotic cell death is present in murine MASH livers of the CDAHFD model, while its inhibition attenuates hepatic lipid accumulation and reduces ALT levels. This implies that ferroptosis might be a detrimental factor in MASH and may become a novel treatment option.

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AN EXTERNAL MULTICENTRIC VALIDATION OF THE IAIHG AUTOIMMUNE HEPATITIS RESPONSE CRITERIA. L. Grossar (1), S. Raevens (2), C. Van Steenkiste (3), I. Colle (4), C. De Vloo (5), H. Orlent (6), J. Schouten (7), M. Gallant (8), A. Van Driessche (9), S. Lefere (1), L. Devisscher (10), A. Geerts (2), H. Van Vlierberghe (2), X. Verhelst (2) / [1] Ghent University Hospital, Ghent, Belgium, Internal Medicine and Paediatrics, Hepatology Research Unit, [2] Ghent University Hospital, Ghent, Belgium, Gastroenterology and Hepatology, [3] Maria Middelares Ziekenhuis, Gent, Belgium, Gastroenterology and Hepatology, [4] ASZ, Aalst, Belgium, Gastroenterology and Hepatology, [5] AZ Delta, Roeselare, Belgium, Gastroenterology and Hepatology, [6] AZ Sint-Jan Brugge-Oostende, Brugge, Belgium, Gastroenterology and Hepatology, [7] AZ Nikolaas, Sint-Niklaas, Belgium, Gastroenterology and Hepatology, [8] Jan Yperman Hospital, Ieper, Belgium, Gastroenterology and Hepatology, [9] AZ Glorieux Ronse, Ronse, Belgium, Gastroenterology and Hepatology, [10] Ghent University, Ghent, Belgium, Basic & Applied Medical Sciences, Gut-Liver Immunopharmacology Unit.

Introduction: The goal of treatment in autoimmune hepatitis (AIH) is induction of remission in order to prevent the development of liver fibrosis, cirrhosis and its related complications. Various definitions of treatment response and remission have been used. Considering the need for consistency in definitions of treatment response, the International Autoimmune Hepatitis Group (IAIHG) recently defined consensus criteria for treatment response. Validation of these criteria is necessary for correlation with hard end points to facilitate comparison between studies.

Aim: To validate the IAIHG response criteria in our cohort and establish correlations with patient survival and survival of the native liver. The primary end point was liver-related mortality. Secondary end points were overall mortality and transplant-free survival.
Methods: We performed a retrospective, multicentric cohort study in one tertiary referral centre, and seven secondary care centres. Case finding was performed by searching the electronic health record database from its inception up to 1 August 2023. Included subjects were in follow-up for a minimum of six months, at least 18 years of age at time of data collection and diagnosed with AIH by a simplified IAIHG score of 6 or more. Patients with features of both AIH and primary sclerosing cholangitis (PSC) or primary biliary cholangiopathy (PBC), as defined by the Paris criteria, were excluded from the analysis. Recorded baseline characteristics included gender, age at diagnosis, follow-up time, presenting symptoms, transaminase levels, and IgG levels at time of diagnosis. Transaminase and IgG evolution were recorded for the first six months of treatment, and during further follow-up when available. Complete biochemical response (CBR) was defined according to the IAIHG consensus criteria as normalisation of transaminases and serum IgG within the first six months of treatment. Time to development of mortality (all-cause and liver-specific) and liver transplantation was calculated and included in time-to-event analysis. Outcome was compared between subjects attaining CBR and those with insufficient response.
Results: Sufficient data were available for evaluation of CBR status in 201 AIH patients of the cohort. Median age at diagnosis and median follow-up were 48 years (range: 5-84) and 7,7 years (range: 0,5-29 years), respectively. There was a female predominance of 147 (73,1%), and 143 individuals (71,1%) were followed-up in a tertiary centre. CBR was achieved in 129 (64,2%) individuals, whereas 72 patients (35,8%) had insufficient response. Non-response, defined as <50% decrease of serum transaminases within 4 weeks after initiation of treatment, occurred in 15 individuals (7,5%). Gender, acute symptoms, and IgG elevation at diagnosis did not associate with CBR status. Liver-related mortality was 6,0% (12 subjects) and all-cause mortality 12,9% (26 subjects). Liver transplantation was performed in 16 individuals (8,0%). In time-to-event analysis, patients achieving CBR exhibited superior liver-related and overall survival, as well as transplant-free survival (p-value for log rank test < 0,001 for all outcomes).
Conclusions: We provide an external validation of the IAIHG consensus criteria for complete biochemical response and correlate them with relevant hard end points in a multicentric, real-world cohort. AIH patients achieving CBR as an intermediate end point have significantly superior patient and native liver survival.

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A NON-INVASIVE SCORE MODEL FOR PREDICTION OF SIGNIFICANT FIBROSIS AND FIBROTIC MASH BASED ON SERUM BIOMOLECULES. N. Beyene (1), W. Kwanten (2), J. Derdeyn (2), T. Steinhauser (2) T. Vanwolleghem (2), A. Driessen (3), S. Francque (2), L. Vonghia (2) / [1] Laboratory of Experimental Medicine and Pediatrics, University of Antwerp, Antwerp, Belgium, Laboratory of Experimental Medicine and Pediatrics, [2] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Department of Gastroenterology and Hepatology, [3] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Department of Pathology.

Introduction: Globally, metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common chronic liver disease. Isolated steatosis (MASL) can progress to metabolic dysfunction-associated steatohepatitis (MASH) with or without fibrosis. Fibrotic MASH (i.e., MASH with ≥ F2 fibrosis) has a higher risk of developing advanced liver disease. The gold standard for identifying MASH and liver fibrosis remains a histological evaluation via liver biopsy, an invasive and costly procedure. Therefore, biopsy- and imaging-free prediction models are still needed to detect liver fibrosis and fibrotic MASH.
Aim: Establishing serum-based non-invasive score model to predict the presence of significant fibrosis (i.e., ≥ F2 fibrosis) in a biopsy-proven cohort of MASLD patients.
Methods: The study included 120 subjects selected from the cohort of patients that underwent a liver biopsy for a suspicion of MASLD at the Gastro-enterology and Hepatology Department of the Antwerp University Hospital. Liver biopsies were stained with H&E and Masson's trichrome. The MASLD activity score (NAS) system was used to determine the histological MASLD features. Besides standard serum biochemistry, serum concentrations of bio-molecules such as cytokeratin-18 (CK-18 M30), tissue inhibitors of metalloproteinases-1 (TIMP1), vascular cell adhesion molecule-1 (VCAM1), and fasting insulin (FI) were determined using an enzyme-linked immunosorbent assay (ELISA). For 53 subjects, the FIB4 index was computed as FIB4= (Age × AST (IU/L)/ (Platelets (109/ L) × √ALT (IU/L). Multivariate analysis was performed to identify independent predictors of fibrosis F≥2 and fibrotic MASH. These variables combined in logistic regression analysis to generate a unique prediction model. Diagnostic performance was then assessed by the area under the receiver operating characteristic curve (AUROC). Using the DeLong test in R via pROC package, the AUROC curves of the newly generated model (Model-B) and liver enzyme-based models (Model-E based on GGT, ALT, AST and age; and Model-FIB4) were compared. P<0.05 was considered statistically significant for all the analyses.
Results: The cohort characterized with an age of 48.6±15 years, a BMI of 35±8.1 kg/m2, and a male-to-female ratio 39%:61%. Histology revealed that 31 of the 120 subjects had no MASL, 31 had MASL, and 58 had MASH; 48 patients had fibrosis F≥ 2, 34 of them had MASH. TIMP1 (OR, 14; CI, 2.7-73; P = 0.02), CK18 (OR, 6; CI, 1.5-24.5; P = 0.011) and FI (OR, 3.7; CI, 1.3-10.3; P = 0.013) were found to be independent predictors of fibrosis F≥ 2, while VCAM1 with

OR 2.6 (CI, 0.85-8.1; P = 0.09). Hence, by integrating TIMP1, VCAM1, CK18 and FI a novel Model-B was established, predicting fibrosis F≥ 2 with an AUROC of 0.95 (CI, 0.91–99, cutoff value is 0.220) with 92% sensitivity and 85% specificity. Model-B predicted fibrotic MASH with an AUROC 0.91 (CI, 0.85–96, cutoff value is 0.202) with 86% sensitivity and 83% specificity. Model-E predicted F≥ 2 with an AUROC of 0.88 (CI, 0.82–0.94, cutoff value is 0.378) with 81% sensitivity and 79% specificity. Model-E predicted fibrotic MASH with an AUROC of 0.80 (CI, 0.72–88, cutoff value is 0.205) with 82% sensitivity and 65% specificity. The Model-FIB4 predicted F≥ 2 with an AUROC of 0.79 (CI, 0.66–0.93, cutoff value is 0.765) with 80% sensitivity and 76% specificity. Model-FIB4 also predicted fibrotic MASH with an AUROC of 0.73 (CI, 0.58–88, cutoff value is 0.765) with 77% sensitivity and 72% specificity. Model-B significantly outperformed Model-FIB4 in the prediction of F≥ 2 (P = 0.037), while there was no significant difference compared to Model-E (P = 0.054). Regarding fibrotic MASH prediction, Model-B was significantly superior to Model-FIB4 and Model-E, P = 0.035 and, P = 0.032, respectively.
Conclusions: A composite score based on serum bio-molecules significantly outperformed scores based on routinely available parameters to identify MASLD-associated significant fibrosis and fibrotic MASH and might be considered as a reliable non-invasive tool, following validation in an external cohort.

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PRE-TREATMENT SERUM N-GLYCANS PREDICT POOR IMMUNOTHERAPY RESPONSE AND SURVIVAL IN HEPATOCELLULAR CARCINOMA. N. Somers (1), E. Butaye (2), L. Grossar (2), H. Van Vlierberghe (2), A. Geerts (2), S. Raevens (2), S. Lefere (3), L. Devisscher (3), L. Meuris (4), N. Callewaert (4), R. Mohr (5), X. Verhelst (2) / [1] Ghent University Hospital, Ghent, Belgium, Gastroenterology and hepatology, [2] Ghent University Hospital, Ghent, Belgium, Gastroenterology and Hepatology, [3] Ghent University, Ghent, Belgium, Basic and Applied Medical Sciences, Gut-Liver Immunopharmacy Unit, Faculty of Medicine & Health Sciences, [4] Ghent University, Ghent, Belgium, Department of Biochemistry and Microbiology, VIB-UGent Center for Medical Biotechnology, [5] Charité University Hospital, Berlin, Germany, Hepatology and Gastroenterology.

Introduction: Patients with hepatocellular carcinoma (HCC) frequently present with advanced disease, for which immunotherapy is the most promising first-line agent – despite the fact that only a quarter of patients show a favourable response. Although serum N-glycans (glycomics) are altered in HCC, they have not been assessed as a predictive marker for treatment response.
Aim: We investigated glycomics as a predictive indicator of poor response to immunotherapy and associated survival in advanced HCC.
Methods: A total of 90 immunotherapy-naive HCC patients were retrospectively recruited with a pre-treatment serum sample. Whole serum N-glycomic analysis was performed using the optimised 96-well on-membrane deglycosylation technique (DSA-FACE). The univariate analysis of survival was calculated by the Kaplan-Meier method and compared by log-rank test. A multivariate Cox proportional hazards model was built to identify independent predictive factors.
Results: This cohort included 90 HCC patients receiving atezolizumab and bevacizumab combination therapy, of which 40 of them had no prior locoregional treatment and were thus completely treatment-naive. Pre-treatment NA3Fc and NA3Fbc glycans were significantly increased in patients who showed poor response (progressive disease) after a median treatment time of 5.9 months as compared with patients who did not. Other independent risk factors were decreased hemoglobin (Hb) and increased aspartate aminotransferase (AST) pre-treatment levels. For the complete treatment-naive patients (n=40) with a baseline GlycanScore (compositescore of NA3Fc and NA3Fbc) above the cut-off value of 1.75, the HR for poor response was 2.16 (95% CI 1.36-3.42, p = 0.001). Combination of this GlycanScore with Hb and AST resulted in the GlycanLabScore with an HR of 2.72 (95% CI 1.677-4.401, p < 0.001) for patients at risk of poor response with low survival (p < 0.001), exceeding the cut-off value of -0.83. Similar findings could be retained when the total cohort was considered, thus including the 50 patients who did receive prior locoregional treatment before the start of immunotherapy. In these patients, the risk for having progressive disease with low survival (p = 0.0017, p = 0.028) was related to a GlycanScore with HR of 1.82 (95% CI 1.40-2.37, p < 0.001) and a GlycanLabScore with HR of 2.63 (95% CI 1.91-3.63, p < 0.001), based on the same cut-off values. In comparison, the alphafetoprotein (AFP) level was not able to significantly differentiate between treatment response, nor could it be included as an independent predictor in the cox regression model for survival prediction.
Conclusions: In this study, we demonstrated that pre-treatment tri-antennary core and branch fucosylated glycans, combined or not with Hb and AST levels, are predictive of poor immunotherapy response and low survival in advanced HCC.

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TRANSITION FROM NON-ALCOHOLIC FATTY LIVER DISEASE TO STEATOTIC LIVE DISEASE: REAL-WORLD EVIDENCE IN A COHORT OF INDIVIDUALS WITH TYPE 1 AND TYPE 2 DIABETES. J. Mertens (1), T. Huybrechts (2), E. Dirinck (3), L. Vonghia (4), K. Wilhelmus J. (5), W. Van Hul (2), C. De Block (3), S. Francque (4) / [1] Antwerp University Hospital, Edegem, Belgium, Endocrinology, Diabetology and Metabolism, [2] Universiteit

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Introduction: A consensus was reached to change the nomenclature and diagnostic criteria of non-alcoholic fatty liver disease (NAFLD) towards the umbrella term steatotic liver disease (SLD), with the inclusion of several sub-categories, based on the presence of cardiometabolic risk factors (Metabolic Dysfunction Associated SLD, MASLD), SLD combined with increased alcohol consumption (metALD) and LSD with co-existence of other liver disease. Real-world data are missing in risk groups to determine the cross-over between the new and old criteria.
Aim: This study aims to examine the diagnostic agreement between both definitions in a cohort of people with type 1 and 2 diabetes.
Methods: This is a retrospective analysis of a large tertiary care center cohort with either type 1 diabetes (T1D), insulin-naïve type 2 diabetes (T2D-IN) or insulin-dependent type 2 diabetes (T2D-ID) prospectively screened for liver steatosis using abdominal ultrasound. Individuals were consecutively invited during their annual check-ups. The only inclusion criterion was having diabetes. All participants were screened for other liver diseases (viral hepatitis, monogenic liver disease, use of steatogenic drugs) and had to fill out a standardized questionnaire to estimate daily alcohol consumption. The diagnosis was based on previous NAFLD guidelines or the new SLD criteria. Prevalence rates were compared. We did not use the cardiometabolic criterion of hyperglycemia/elevated HbA1c/antidiabetic treatment in subjects with T1D, due to their auto-immune etiology of hyperglycemia.
Results: A total of 1177 individuals were included: 661 patients with T1D, 248 with T2D-IN, and 268 with T2D-ID. Steatosis was present in 118/661 individuals with T1D (17.9%). Based on the criteria for NAFLD, 109 individuals had NAFLD (16.5% of total, 92.4% of people with steatosis). According to the new criteria, 109 subjects had MASLD, while 5 had metALD (0.8%). Four subjects (0.3%) had a combination of MASLD with another cause other than alcohol (steatogenic drugs in all 4). In those with T2D-IN, steatosis was present in 159/248 individuals (64.1%). NAFLD was present in 151 individuals (60.9% of total, 95.0% of people with steatosis). MASLD was present in 151 subjects (60.9%), while 5 subjects had metALD (2.0%), and 4 (1.6%) had MASLD combined with another etiology (steatogenic drugs n = 3, hepatitis B n = 1). In people with T2D-ID, 171/268 had steatosis (63.8%). NAFLD was present in 150 subjects (56.0% of all, 87.8% of those with steatosis). MASLD was present in 150 cases (56.0%). MetALD was present in 10 subjects (3.7% of cases), 11 people (4.1%) had MASLD combined with another etiology (steatogenic drugs n = 4, viral hepatitis n = 6, alfa-1 antitrypsin deficiency n = 1). The generally low prevalence of metALD could be explained partially due to participation bias.
Conclusions: Liver steatosis is common in people with T1D, and highly prevalent in people with T2D, regardless of the use of insulin. Agreement between NAFLD and MASLD was 100% in subjects with T1D, T2D-ID, or T2D-IN.

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THE TOULOUSE ALGORITHM IDENTIFIES PATIENTS WITH AN INCREASED RISK OF CARDIAC DECOMPENSATION ONLY IN PATIENTS WITH TIPS FOR REFRACTORY ASCITES.

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Introduction: Transjugular intrahepatic portosystemic shunt (TIPS) placement is an effective, possibly life-saving, treatment for complications of portal hypertension. The pressure shift induced by the stent can lead to the development of cardiac decompensation (CD) in some cases.
Aim: We investigated the incidence of CD, possible variables associated with CD and the validity of the Toulouse algorithm for risk prediction of CD post-TIPS.
Methods: All patients receiving TIPS for variceal bleeding (VB) or refractory ascites (RA) between 2011 and 2021 were retrospectively reviewed. A total of 106 patients (41.5% VB, 58.5% RA) had echocardiography and NT-proBNP results available and were included. Development of CD between time of TIPS placement and occurrence of liver transplantation, death or loss-to-follow-up was recorded. Competing risk regression analysis was performed to assess which baseline variables predicted occurrence of CD post-TIPS.
Results: A total of 12 patients (11.3%) developed CD after a median of 11.5 days (IQR 4 to 56.5) post-TIPS. Multivariate regression showed age (HR 1.06, CI 1.01-1.11, p 0.019), albumin (HR 1.10, CI 1.03-1.18, p 0.009) and NT-proBNP (HR 1.00, CI 1.00-1.00, p 0.023) predicted CD in the RA group. No clear predictors were found in those receiving TIPS for

VB. Correspondingly, the Toulouse algorithm successfully identified patients at risk for CD, however only in the RA population (zero risk 0% vs. low risk 12.5% vs. high risk 35.3% with CD; p 0.003).
Conclusions: CD is not an infrequent complication post-TIPS occurring in 1/10 patients. The Toulouse algorithm can identify patients at risk of CD, though only in patients receiving TIPS for RA. Allocation to the high-risk category warrants close monitoring but should not preclude TIPS placement.

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DEVELOPMENT OF MICROENVIRONMENT-DEPENDENT HEPATOCELLULAR CARCINOMA AND COLORECTAL LIVER METASTASIS SPHEROID CULTURE MODELS. E. Knetemann (1), A. Herrero (2), L. van Grunsven (3), I. Mannaerts (3) / [1] Vrije Universiteit Brussel (VUB), Jette, Belgium, Liver Cell Biology Research group, [2] University of the Basque Country, Spain, Department of Cell Biology and Histology, [3] Vrije Universiteit Brussel (VUB), Jette, Belgium, Liver Cell Biology Research Group.

Introduction: Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer. It is currently the third leading cause of cancer-related deaths. The liver is also very prone to the development of metastasis which are associated with only a one-year survival rate of 15%. Colorectal cancer liver metastases (CRLM) are particularly common with 35-55% of colorectal cancer patients developing liver metastases at some point during the disease. One of the reasons for failure of therapeutic compounds in clinical trials is the lack of relevant preclinical in vitro models. Both 2D and 3D culture models consisting solely of (cancer) cell lines are often used, although these models cannot accurately recapitulate the in vivo microenvironment.
Aim: We aim to develop 3D in vitro culture models for HCC and CRLM in which we can investigate cell communication between liver-resident cells and cancer cells.
Methods: Freshly isolated mouse hepatocytes, hepatic stellate cells (HSC), liver sinusoidal endothelial cells and Kupffer cells were obtained by liver perfusion and digestion using collagenase and pronase followed by a Percoll gradient to further isolate and purify the hepatocytes and flow cytometry for the isolation of the other liver cell types. The liver cells were then mixed with either a mCherry-labelled mouse hepatoma cell line (Hepa1-6) or mouse colon adenocarcinoma cell line (MC-38) and seeded in cell-repellent plates to generate scaffold-free spheroids. We can generate 600 of such multicellular spheroid cultures from one mouse liver. The spheroids were maintained in serum-free medium throughout the rest of the culture. Fluorescence microscopy was used to determine cancer cell proliferation. Cell viability assays, picrosirius stainings and qPCR analysis for HSC activation markers were carried out on day 2 and/or day 7 of culture.
Results: At the moment of spheroid seeding, 10 cancer cells are added to the mix of primary liver cells to form a spheroid. Over a period of 7 days, these cancer cells grow rapidly inside the liver spheroid as demonstrated by the increase in mCherry positive cells. In contrast, when cancer cells are seeded alone as spheroids in the same serum-free medium, the cells fail to thrive as evidenced by increased cell death and reduced cell growth. Importantly, the addition of cancer cells appears to induce a fibrotic response in the spheroids as shown by increased collagen deposition and increased mRNA levels of HSC activation markers in the spheroids.
Conclusions: By including four liver cell types freshly isolated from mouse livers as well as cancer cells, we have developed new relevant models to study HCC and CRLM. We could demonstrate that in these spheroid cultures, the liver microenvironment is essential for the support of liver cancer cell growth. Furthermore, we show that these cultures have the potential to mimic HSC to cancer associated fibroblast transdifferentiation. In the future, this model could be used as a screening tool for potential drug candidates before moving to in vivo models. This could greatly decrease the number of mice used in preclinical research and enhance the predictability of preclinical screens.

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LIVER ELASTICITY EVOLUTION IN METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE PATIENTS: A REAL-LIFE PROSPECTIVE STUDY. J. Scholtens (1), S. André-Dumont (1), G. Henin (1), G. Dahlqvist (1), N. Lanthier (1) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'Hépato-Gastro-Entérologie.

Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD) has become the first cause of chronic liver disease worldwide with a variable course over time. There is little prospective data on the long-term follow-up of these patients.
Aim: The aim of our study is to evaluate the evolution of liver disease, in real life, using hepatic elastometry by identifying patients who will improve or progress over time.
Methods: This is a prospective, single-centre study including patients with MASLD. Transient elastography was performed at baseline and checked after one (Y1) and three years (Y3). Patients were stratified into three groups based on the evolution of liver elasticity. Regression or progression of liver disease were defined as a decrease or increase in liver elasticity of > 1.5 kPa compared with baseline value. Stable patients are those with elasticity changes ≤ 1.5 kPa.

Results: 229 patients were included (126 women and 103 men) with the following characteristics: mean age 52 years, mean body mass index 33.9 kg/m², significant proportion (98%) with an enlarged waist circumference (F ≥ 80 cm; M ≥ 94 cm) and a mean of 114 centimetres, 20 patients (9%) had an history of cardiovascular events, 86 patients (38%) were treated for type 2 diabetes. The baseline mean liver elasticity was 10.5 kPa (± 8.8) and the mean controlled attenuation parameter (CAP) was 331.1 dB/m (± 43.5). 100 patients (44%) were classified as F0-F1, 64 (28%) as F2, 43 (19%) as F3 and 22 (10%) as F4. Most received lifestyle advice by the hepatologist (n=157, 69%), others underwent bariatric surgery (n=30, 13%), were either included in an interventional clinical study in the context of MASLD or metabolic syndrome (n=21, 9%) or referred to the dietitian (n=18, 8%). 146 patients (64%) and 110 patients (48%) underwent follow-up elastography at one and three years respectively. Mean liver elasticity (Y0: 10.5, Y1: 7.8, Y3: 7.9 kPa; p=0.0008) and CAP (Y0: 331.1, Y1: 307.1, Y3: 317.4 dB/m; p=0.0007) decreased over time. At Y1, a minority of patients were progressors (n=26, 18%), 71 (49%) remained stable, and 49 (34%) exhibited improvement in liver elasticity. After three years (Y3), 21 (19%) experienced progression, 43 (39%) remained stable, and 46 (42%) demonstrated improvement. Interestingly, compared with progressors (P) or stable patients (S), improvers (I) at Y1 exhibit a more severe condition at baseline (Y0), characterized by higher BMI (I: 34.6, S: 31.7, P: 32.5 kg/m²; p=0.05), waist circumference (I: 116, S: 108, P: 110 cm; p=0.0048), fasting glucose (I: 125, S: 105, P: 110 mg/dL; p=0.0015), low HDL (I: 43, S: 52, P: 51 mg/dL; p=0.0157), elasticity (I: 12.2, S: 6.6, P: 7.5 kPa; p<0.0001) and CAP values (I: 343, S: 322, P: 328 dB/m; p=0.05). The same is also true for Y3 vs. baseline (Y0) with additionally an elevated mean AST at Y0 (I: 47, S: 34, P: 39 UI/L; p=0.0012). The improvement in this group is associated at Y1 with a significant BMI reduction (-3.7 kg/m²; -9%) compared with stable patients (-1.1 kg/m², -2.6%) and progressors (-0.1 kg/m², -0.4%) (p=0.0003). At Y3, improvers had also a significant BMI decrease (-2.1 kg/m²; -6%) compared with stable patients (-0.6 kg/m², -1.7%) and progressors (+0,6 kg/m², +1.7%) (p=0.0005). All the patients who underwent bariatric surgery demonstrated disease regression at either one or three-year follow-up, however more than the half (Y1 vs. Y0: 60%, Y3 vs. Y1: 50%) of lost to follow-up patients was seen in this category. Among the events occurring during follow-up, 11 patients developed diabetes, 2 had hepatocellular carcinoma and 2 experienced a cardiovascular event.
Conclusions: These are the first prospective data on the evolution of liver elasticity in MASLD patients. Standard hepatological management can have an impact on liver disease, interestingly, particularly in patients with severe initial MASLD. We confirm that a 6 to 9% of loss in BMI is associated with a regression in hepatic elasticity, consistent with regression of fibrosis. Patients who progress represent a fifth of population and are easily identified by the absence of weight loss over time. So, the focus should be on weight reduction.

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GUT MICROFLORA COMPOSITION IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE. T. Khachidze (1), G. Barbakadze (2) / [1] Grigol Robakidze University, Tbilisi, Georgia, Gastroenterology and Hepatology, [2] Grigol Robakidze University, Tbilisi, Georgia, Gastroenterology.

Introduction: Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in developed countries and affects about 25-30% of the population. An increasing number of studies have indicated a close relationship between dysbiosis and NAFLD. Hence, there is an interest in exploring the fatty infiltration as the result of the dysbiosis, that includes bacterial composition disturbance, with profound analysis of preventive and aggressive factors that impact on liver disease occurrence and progress.
Aim: The aim of this study was to analyze the gut microbiota composition in patients with NAFLD with possible examination of aggressive and protective factors, including small intestinal bacterial overgrowth existence and biochemical markers
Methods: This study recruited 93 subjects with median age of 58 (22–78) diagnosed with NASH/NAFLD based on a fibro scan of the liver, ultrasound and biochemical tests. The criteria for fatty infiltration existence was a diffuse increase in the echogenicity of the liver parenchyma, decreased attenuation on the liver and ratio between the brightness level of the liver and the right kidney that was calculated for the hepato-renal index (HRI) determination. Biochemical evaluation included liver functional tests lipid profile. Stool sample examination was performed using Real time-PCR. glucose hydrogen breath test was performed to all patients
Results: The study's findings were as follows: A 55.1% correlation was found between NAFLD and SIBO in the gut microbiome. The following bacteria were present in the microbiota in the following proportions: Firmicutes (46.3±1.99), Actinobacteria (26.1±18), and Firmicutes/Bacteroidetes ratio (F/B)-5.99±1.85). Bacteroidetes and Firmicutes had a markedly negative connection (r = -0.89), as did the Bacteroidetes and Firmicutes/Bacteroidetes index (r = -0.74) and Bacteroidetes and Actinobacteria (r = -0.90). Additionally, there was a significant positive association between the F/B index and ALT (r = 0.5) and triglycerides (r = 0.52). Also, there was a middle-strong connection (r = 0.43) between the presence of SIBO and the growth of Firmicutes in NAFLD patients.
Conclusions: According to the study, increased Firmicutes and Actinobacteria are caused by decreased levels of Bacteroidetes, which raises triglycerides and ALT levels in patients with NAFLD and is associated with SIBO. The F/B index may be a marker for the presence of NAFLD, while Bacteroidetes may act as potential inhibitors of NAFLD progression. Patients with NAFLD should be tested for SIBO, and vice versa.

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PREVALENCE OF HCV, HBV AND HIV IN A PSYCHIATRIC CENTRE IN BELGIUM. L. Seynhaeve (1), J. Decaestecker (2), C. De Vloo (2), L. Harlet (2), J. Dewyspelaere (2), W. De Troyer (3), K. Neyrinck (3), K. Ferdinande (2) / [1] AZ Delta, Roeselare, Belgium, Maag-darm-lever, [2] AZ Delta, Roeselare, Belgium, Gastroenterology, [3] Psychiatrisch Centrum O.L.V. van Vrede Menen, Menen, Belgium, Psychiatry.

Introduction: The prevalence of HCV, HBV and HIV is estimated to be higher in patients with severe mental illness compared to the general population. These higher prevalence rates are often due to multiple factors such as more drug and alcohol abuse and sexual risk behavior. Although there is no national screening program in Belgium, the WHO keeps setting the goal to eliminate viral hepatitis by 2030. Therefore, micro-elimination projects could help to reduce the incidence of these diseases.
Aim: The aim of this project was to measure the prevalence of HCV, HBV and HIV in a local psychiatric centre in Menen (PCM) (233 licensed beds) and to demonstrate the utility of structural screening within an at-risk population in the context of secondary prevention.
Methods: Between April 2021 and December 2022, an ICF was administered to newly admitted patients by the intake nurses at the PCM. In it, permission was requested to determine HCV, HBV and HIV status in addition to the standard blood sampling done on admission; and to complete a questionnaire surveying participants' risk behaviour. The questionnaire consisted of a listing of the various risk factors where participants could tick 'yes', 'no', 'don't know' or 'won't answer'. Inclusion criteria: Age 18 years and above Able to complete a questionnaire
Results: We've asked 236 patients if they wanted to particpate. 71 of them refused to participate or we received an incomplete file so we could not include these patients. We've screened 165 patients on these 3 blood borne viruses. 4 patients were positive on HCV antibodies but none of them had a positive HCV PCR. No patient was positve on HIV antibodies. No screened patient was positive on HbsAg so none of them had positive chronic hepatitis B. There were 46 patients with positive HbsAB (≥10 IU/L) of which 2 patients had positive HbcAb. 28 of the screened patients had elevated ALT and/or AST tests. Many risk factors were present in the screened population: 35% of patients reported ever injecting or sniffing drugs, 24% were babyboomers, 18% reported having frequent unsafe sex, 17% had ever been in prison, 16% were victims of rape, 11% had ever received a blood transfusion before 1990, 8% had a tattoo or piercing done in unsanitary conditions, 4% of the patients were men who have sex with men and only 1% of the patients surveyed were migrants from a country with high prevalence rates of these blood-borne viruses. Of the four patients with positive hepatitis C antibodies, two patients were classified on a DSM IV base with a 'substance-related disorder', one patient with a 'delirium, dementia and amnestic and other cognitive disorder' and one patient with a 'disorder usually first diagnosed in infancy, childhood or adolescence'.
Conclusions: Scientific literature suggests that the prevalence of HCV, HBV and HIV in patients with mental illness is higher compared to the prevalence in the general population, This is not due to the mental illness itself, but rather because high-risk behaviour is often exhibited by this patient group. There is a higher prevalence of HCV and HBV in this sample compared to the general population. But not as high as the reported prevalence. Well-organised screening within certain high-risk groups is a good tool for Belgium if it wants to meet the WHO goal of eliminating viral hepatitis by 2030. This sample is rather small so the results may differ from the existing literature. There may also be a selection bias in this study as patients were given the choice to participate in the study. Thus, patients who know they were at-risk could refuse to participate. Based on this study, the prevalence of HCV, HBV and HIV in the PCM appears to be lower than the European prevalence rate in patients with mental illness. Patients who were screened exhibited high risk behaviour which does lead to higher prevalence rates of HCV and HBV (not HIV) compared to the general population. Structural screening within this patient group does not seem cost-effective based on our sample. However, one can, for example, examine within which psychiatric diagnoses the prevalence is higher. More research is needed.

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LONG-TERM HISTOLOGICAL FIBROSIS REDUCTION FOLLOWING SVR IN HCV-RECURRENCE AFTER LIVER TRANSPLANTATION. T. Lemmens (1), G. Henin (1), S. Aydin (2), P. Baldin (2), Y. Horsmans (3), G. Dahlqvist (1) / [1] UCL Saint Luc, Brussels, Belgium, Service d'Hépato-Gastro-Entérologie, [2] UCL Saint Luc, Brussels, Belgium, Service d'Anatomopathologie, [3] UCL Saint Luc, Brussels, Belgium, Service d'Hépato-Gastro-Entérologie.

Introduction: Fibrosis regression has been observed on native livers after obtaining sustained virological response (SVR) in hepatitis C (HCV), abstinence in alcoholic liver disease (ALD) and bariatric surgery in metabolic associated steatotic liver disease (MASLD). However, in liver transplant (LT) recipients, data are scarce. In addition, most data come from studies using non-invasive measurements to evaluate liver graft fibrosis, while these aren't validated in this situation and are also limited by typical post-LT complications (biliary stenosis, outflow syndrome, etc.). HCV recurrence after LT is universal if HCV RNA persists at time of LT and progression to fibrosis is rapid. Nowadays, HCV is systematically eradicated with direct acting antivirals (DAA). SVR is obtained in > 95% of patients with a native liver or after LT. Data remain scarce on fibrosis evolution after DAA treatment and long-term evolution (>5-10 years). Since

SVR is now almost universal, HCV eradication after recurrence on the liver allograft seems to be an interesting model to study fibrosis regression because of the availability of protocolar liver biopsies.
Aim: We wanted to evaluate the evolution of allograft fibrosis after reaching SVR in transplanted patients with HCV recurrence that were followed with protocol-based liver biopsies. We compared this cohort with a control group consisting of non-viral transplant recipients who did not experience a recurrence of the initial disease and underwent similar protocol-driven paired liver biopsies. Our hypothesis was that HCV elimination would lead to a decrease in fibrosis on the long term, in contrast with the control group where we anticipated a natural slow progression of fibrosis.
Methods: We performed a retrospective monocentric cohort study in which we evaluated all patients with recurrent HCV after LT obtaining SVR after treatment from 2011 until 2020. We obtained approval from the ethics committee. We collected patients' data at the time of transplantation, HCV treatment and at follow-up protocolar liver biopsies. We compared liver biopsies that were realized before HCV treatment, at a short-term follow-up (1-2 years) and a long-term follow-up (>3 years). We evaluated fibrosis on Massons' trichrome slices, with METAVIR- and LAF-scores. We conducted Picro-sirius red staining to identify collagen fibers, enabling a semi-quantitative assessment of fibrosis. We reported the fibrosis as a percentage of the overall liver area. As a control group, transplanted patients for polycystic liver disease, ALD without recurrence and congenital liver disease (biliary atresia) were selected. We matched our patients on a 1/1 basis with pairing for time interval of liver biopsies from liver transplantation.
Results: A total of 32 patients were treated with IFN (n=4) or DAA (n=28) for recurrent HCV infection of the liver allograft. Eight patients were excluded because they did not have any post treatment liver-biopsy and 5 because histological data was of insufficient quality (< 5 portal tracts). The 19 remaining patients had an SVR of 100%, 17 with DAAs and 2 with IFN. In the study patients, fibrosis regression was present in 47% of patients and statistically significant on the long term (> 3 years) according to the METAVIR score (-0.8; $p < 0.01$) and the LAF score (-1.5; $p < 0.02$). Sub analysis of the LAF-score showed significant reduction of fibrosis in the portal ($p < 0.04$) and sinusoidal ($p < 0.003$) areas, but not in the centrilobular area. These results were confirmed by reduction in the total fibrosis area by a mean of 5.9% ($p < 0.002$). Reduction of fibrosis was not significant on the short term (<2 year follow-up). There was no statistical difference between the HCV group and the control group. The control group progressed over the same follow-up period with a mean of 0.66 METAVIR compared to a reduction of 0.8 METAVIR in the HCV group ($p < 0.001$).
Conclusions: In this retrospective study, we show that achieving SVR following HCV elimination in allograft recipients leads to long-term improvement in histological fibrosis. This was confirmed by a semi-quantitative assessment of collagen fibers. Additionally, our findings highlight a significant reduction in fibrosis compared to the control group in which we confirm a natural and slow progression of fibrosis on the allograft.

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HEPATITIS C AMONG DRUG USERS IN CHARLEROI: THE OTHER SIDE OF THE OPOID CRISIS. H. Cherkaoui (1), E. Toussaint (2), D. Blero (2), W. Soub Defeu (2) / [1] Hôpital Civil Marie Curie, Lodelinsart, Belgium, Gastro enterologie, [2] Hôpital Civil Marie Curie, Lodelinsart, Belgium, Gastroenterology.

Introduction: Hepatitis C is a frequent and silent disease among intravenous drug users (IDU). It's a disease with societal implications in these communities. The direct acting anti-virals allow a good eradication rate of hepatitis C.
Aim: We aimed to determine the response of drug users to direct acting anti-virals and determine the response factors
Methods: We conducted a hepatitis C screening campaign among intravenous drug users (IDU). It's a prospective study (September 2020-September 2023) performed at the Diapason drug shelter by general physicians and gastro-enterologists. All data was gathered using an excel sheet and statistical analysis was performed using SPSS v 22.
Results: Forty-four patients were included in the study among intravenous drug users; they were screened and treated for hepatitis C. The median age was 42 y/o, and SR M/ F was 9. The predominant intravenous drug was Heroin (52%). Most patients were asymptomatic, the most common genotype was 3A, and the median viral load was 2.61 Log. All patients were put on direct antivirals as first-line (95%) or second-line (5%). The most frequent antivirals were: glecaprevir pibrentasvir (55%), 13% on sofosbuvir velpatasvir, and 12% had an initial negative viral load. The antiviral regimen was completed in 77%. Among those who completed the antivirals, the eradication rate was 92%. A negative viral load was found in 50 % of those who didn't finish the antivirals. Among drug users, glecaprevir pibrentasvir was the antiviral of choice to achieve a negative viral load (p: 0,001). The main factors associated with hepatitis C recurrence were Heroin abuse (p: 0,02) and hepatitis B infection (p: 0,016).
Conclusions: Overall, it was a human and enriching experience for the gastroenterology department at the University Hospital of Charleroi. Seeing the community's challenges and allowing our medical practice to be outside hospital walls was eye-opening for the team. It was an excellent way of conducting community service in the best way we know. The patient's compliance was unexpected (72%), with a negative viral load in 92% of the patients. The best treatment regimen in our experience was glecaprevir pibrentasvir, as fibrosis was rarely found, treatment was taken for only eight weeks, and overall drug interactions.

HEPATITIS C: DIFFERENCES BETWEEN THE NORTH AND THE SOUTH. H. Cherkaoui (1), N. Lahmidani (2), A. Mekkaoui (2), D. Benajah (2), S. Ibrahimi (2), M. Abkari (2), E. Toussaint (3), W. Soub Defeu (3), H. Abid (2) / [1] Hôpital Civil Marie Curie, Lodelinsart, Belgium, Gastro-Entérologie, [2] University Hospital Hassan II, Fez, Morocco, Gastroenterology, [3] Hôpital Civil Marie Curie, Lodelinsart, Belgium, Gastroenterology.

Introduction: Since the advent of direct antivirals, the treatment of hepatitis C has undergone a revolution worldwide. The WHO's goal is to eradicate hepatitis C by 2030. Hence the interest of our study is to compare the results of hepatitis C eradication between two countries with different economic contexts.
Aim: The aim is to determine the eradication rate between the two population as well as predictive response factors to direct acting anti-virals between the two populations.
Methods: This is a retrospective study of an extensive series of hepatitis C cases collected over ten years between the University Hospital of Charleroi, Belgium, and the Hassan II University Hospital of Fez, Morocco. Our objective is to compare the characteristics of the two hepatitis C populations and the results of viral eradication under direct antiviral therapy. All data was gathered on an excel sheet and statistical analysis was performed using SPSS v.22
Results: We collected 287 patients, of which 162 were Moroccan (group M), and 205 were Belgian (group B). The average age at diagnosis was 53 years (55 years in group M and 49 years in group B). Cirrhosis was diagnosed in 43% of Group M and 12% of Group B. Excessive alcohol consumption was noted in 6% of Group M and 20% of Group B. Asthenia was the most frequent clinical sign (55% in Group M and 65% in group B). Biology showed thrombocytopenia (10% in group M and 2.4% in group B), low PT (6% in group M and 4% in group B), cytolysis (5% in group M and 20% in group B), elevated GGT (5% in group M and 4% in group B). Co-infections were present in both populations: HBV co-infection (5% group M, 3% group B), HBV cured profile (3% group M, 2% group B), and HIV (1% group M and 2.4% group B). The most frequent genotype in both populations was genotype 1b (35% in group M and 28% in group B). The mean viral load before treatment was 6 logs in group M and 5 in group B. Fibroscan showed significant fibrosis in 44% of group M and 12% in group B. A liver biopsy was performed in 6% of both groups following a discrepancy between fibroscan and fibrotest. In cirrhotic patients, gastroscopy found VO in 12% of cases (group M) versus 4% of group B, portal hypertension gastropathy in 2% of group M and 4% of group B. The most common treatments used in both groups were sofosbuvir velpatasvir (39% group B) for 12 weeks, sofosbuvir daclatasvir +/- ribavirin for 12 weeks (29% group M versus 3% group B), sofosbuvir ledipasvir (27% group M), glecaprevir pibrentasvir for eight weeks (58% group B), a combination of pegylated interferon and ribavirin (44% group M); The eradication rate in group M was 69% (55% in patients on ribavirin and 98% in patients on direct antivirals). In group B, the eradication rate was 92% (all patients were on direct antivirals). The use of direct antivirals is a good factor of therapeutic response in group M (p: 0.01), and group B (0.02) cirrhosis is a factor of poor therapeutic response in group M whatever the prescribed therapeutic regime.
Conclusions: Through this work, we notice that the difference between the eradication rate between group M and B are the presence of post-viral cirrhosis C and ribavirin use. Those factors were predominant in population M compared to population B.

FACTORS IN POOR RESPONSE TO URSODESOXYCHOLIC ACID IN PRIMARY BILIARY CHOLANGITIS. H. Cherkaoui (1), N. Lahmidani (2), A. Mekkaoui (2), D. Benajah (2), M. El Yousfi (2), S. Ibrahimi (2), M. Abkari (2), H. Abid (2) / [1] Hôpital Civil Marie Curie, Lodelinsart, Belgium, Gastro-Entérologie, [2] University Hospital Hassan II, Fez, Morocco, Gastroenterology.

Introduction: Primary biliary cholangitis (PBC) is a cholestatic disease that affects the small bile ducts and can progress to cirrhosis.
Aim: This study aims to determine the factors of poor response to AUDC to quickly change the therapeutic line and slow down the evolution toward liver transplantation.
Methods: This is a retrospective monocentric study of all PBC cases followed up in extended consultation over 23 years (1999-2022). The response to AUDC was evaluated according to the Paris II criteria and patients were divided into two groups according to their response to AUDC. Data were collected in Excel and statistical analysis was performed with SPSS software.
Results: 59 patients were enrolled. The mean age of the patients was 58 years (24-83 years), with a female predominance of 92.1%. 38.9% of patients were diagnosed with cirrhosis. Clinical manifestations were pruritus (49%), asthenia (29%), and abdominal pain (13%). GGT at admission was greater than 3N in 84% of patients and PAL greater than 2N in 75% of patients. Anti-mitochondrial M2 antibodies were positive in 94% of patients. An overlap syndrome associating PBC, and autoimmune hepatitis was found in 24.3% of patients. A liver biopsy was performed in 24% of patients. All patients were put on AUDC, associated with cortisone therapy in patients with an overlap syndrome. A response to treatment at one year was found in 68% of patients. In multivariate analysis, the elements associated with poor therapeutic response were hyperbilirubinemia (p=0.002), cirrhosis at the time of diagnosis (p=0.01), and an elevated LAP level (p=0.04), elevated GGT level (p= 0.02), and overlap syndrome (p=0.03).

Conclusions: The identification of these factors would allow a rapid change of therapeutic line in patients with PBC to slow down the progression towards liver transplantation as this technique is not always available in our context.

- A40 -

METABOLIC ASSOCIATED STEATOHEPATITIS IS ASSOCIATED TO NO-DEPENDENT ENDOTHELIAL DYSFUNCTION IN MICE. J. Lallement (1) / [1] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, IREC/GAEN.

Introduction: Metabolic dysfunction-associated fatty liver disease (MAFLD) affects 25% of the World's population, with 20-50% of cases progressing to steatohepatitis (MASH for metabolic associated steatohepatitis) and eventually cirrhosis. MAFLD, and more so MASH, confers a superimposed risk to develop cardiovascular diseases (CVDs) and to die prematurely. Although numerous clinical studies have demonstrated a robust association between MASH and CVDs, independent of dysregulated metabolism and obesity, the pathogenic mechanisms supporting a liver to CVD axis remain poorly understood. Endothelial dysfunction is a vascular disease that affects the endothelium of arteries and arterioles. In this pathology, imbalanced production of relaxing and contracting factors by endothelial cells impairs regulation of vascular tone in favor of vasoconstriction. Endothelial dysfunction is an early feature of atherosclerosis and hypertension that could induce heart failure. Interestingly, MAFLD/MASH patients are at greater risk of developing endothelial dysfunction.
Aim: The goal of this study is first to characterize the vascular system with a special focus on endothelial function in a murine model of MASH disease. Secondly, we aim to decipher altered signaling pathways that contribute to endothelial dysfunction as well as the contribution of MASH in this alteration.
Methods: We used male non-obese (NOD.B10) fat aussie (Foz) mice, bearing a homozygous truncating mutation in the Alms1 gene, fed with high fat diet (HFD, 60 kcal% from fat) as a model of MASH disease. These mice are hyperphagic and display a fibrosing MASH after 24 weeks of HFD. The littermate also fed with HFD exhibit mild steatosis and mild metabolic disturbances and were used as MAFL (no MASH) controls. Blood pressure was measured during 24h (3 times) by telemetry and we investigated the presence of atherosclerotic plaques in the aorta using red oil staining. Endothelial function was assessed in first order mesenteric arteries by wire myograph measurements. In order to isolate the nitric oxide (NO)-dependent component of the relaxation, vessels were incubated in the presence of inhibitors blocking prostacyclin and EDHFs (endothelium-derived hyperpolarizing factors)-dependent relaxation. Nitrosylated hemoglobin (HbNO) in the blood was measured by electron paramagnetic resonance. Asymmetric dimethylarginine (ADMA), an endogenous inhibitor of NO production, was quantified using fast ELISA according to manufacturer's specifications. Western blot analysis and qPCR were performed for investigations of the NO pathway in the liver and aorta.
Results: Despite the absence of atherosclerotic plaques and hypertension, HFD-fed Foz mice (FH) exhibit endothelium-dependent impaired relaxation in first order mesenteric arteries. By using PGI2- and EDH(Fs) inhibitors, we demonstrated reduced NO-dependent vasodilatation in response to carbachol in FH compared to HFD-fed controls (WH). Consistent with these data, our results indicate reduced phosphorylation on serine 1177 of endothelial nitric oxide synthase (eNOS) in the aorta of FH, reflecting less activation of this enzyme. No alterations were observed in the gene expression of eNOS or its inhibitor Cav1. ADMA levels were also higher in FH plasma than in WH plasma. Surprisingly, there was no difference in blood HbNO between these two groups. The hepatic expression of inducible NO synthase (iNOS), induced by inflammation as in MASH liver, is significantly increased in FH compared to WH (fold change 15, p-value: 0.002).
Conclusions: Taken together, our results show that mice with MASH but not those with MAFLD exhibit endothelial dysfunction with impaired NO-dependent vasodilation which could be caused in part by lower activation of eNOS and elevated plasma ADMA level. Our data also suggest that the inflamed liver could contribute, via the up-regulation of iNOS expression, to the alteration of the NO balance by disturbing systemic NO production. These findings underline the importance to unraveling the liver-vessel-heart crosstalk to better understand the pathophysiological substratum for MASH-driven increased of the CV risk.

- A41 -

HEPATITIS C LOST-TO-FOLLOW-UP IN PRIMARY CARE - HELP PROJECT. M. Coessens (1), J. Schouten (1), W. Verlinden (1) / [1] Vitaz, Sint-Niklaas, Belgium, Gastroenterology and Hepatology.

Introduction: Hepatitis C virus (HCV) infection is a major global health problem. Since the development of the direct-acting antivirals (DAA), HCV is regarded a curable disease. In 2015, the number of chronically infected persons in Belgium was estimated at 18 800 and we need to treat at least 1200 patients per year to eliminate HCV as a public health threat by 2030. Cost-effective approaches are needed to reach these goals, including lost-to-follow-up (LTFU) strategies. Our research group has already established LTFU rates of 16-19% in hospital-based LTFU projects, with up to half of the patients who had dropped out being successfully re-admitted into care. The 2016 "save your liver"-barometer showed a knowledge gap on HCV in the Belgian general practitioner (GP) population. Therefore, it is of interest to assess LTFU rates in a primary care population.

Aim: This is the first Belgian project to assess LTFU rates in the GP/primary care population. The secondary aim is to encourage patient reintroduction into the HCV care continuum through the GPs, also for patients who previously did not meet the DAA reimbursement criteria due to absence of advanced fibrosis.
Methods: This study was carried out in cooperation with AML (Algemeen Medisch Laboratorium, a peripheral laboratory in Antwerp). AML compiled a list of all positive HCV serology results requested between 2010 and 2023 by a general practitioner based in Antwerp (Antwerpen, Berchem, Borgerhout, Deurne, Hoboken, Merksem, Wilrijk, Zwijndrecht/Burcht). AML reached out to the GPs by letter and phone to inquire about their participation. The GPs that agreed to participate in the HeLP-project, were contacted by a member of the study team to go over the patient list. Patient status in the hepatitis C care continuum was defined as follows; (a) false positive HCV serology (Chemiluminescence Microparticle Immuno Assay, Abbott Architect and Fluorescence Enzyme Immuno Assay, Vidas), (b) borderline HCV serology in combination with negative HCV RNA, (c) positive HCV serology in combination with the last HCV RNA being negative, (d) possible chronic HCV in case of a positive HCV serology without an available HCV RNA, (e) chronic HCV when the last available HCV RNA was positive, (f) possible chronic HCV if HCV RNA was negative <12 weeks after end of treatment (EOT), (g) cured HCV infection if HCV RNA was negative ≥12 weeks after end of treatment, sustained virological response (SVR), (h) deceased. The patient was considered LTFU if no action was taken in case of status d, e, or f.
Results: In total, 167 out of 275 (60,73%) primary care physicians agreed to participate. Participation rates were lower in the north of Antwerp (44.29%, p=0.001). In total, 366 primary care patients were analysed for their status in the HCV care continuum [(a) 94/366 (25.68%); (b) 5/366 (1.37%); (c) 120/366 (32.79%); (d) 15/366 (4.10%); (e) 33/366 (9.02%); (f) 5/366 (1.37%); (g) 79/366 (21.58%); (h) 15/366 (4.10%)]. Overall, the rate of lost-to-follow-up in primary care was 53 out of 366 or 14.48 %. In 2 areas, lost-to-follow-up rates were already re-assessed one year after the LTFU project started. Here, eight patients were LTFU [(e) untreated chronic HCV infection, 5/8; (f) negative HCV RNA at EOT, 3/8]. One year later, 4 out of 8 patients have taken 1 or more steps forward in the HCV care continuum [(e) untreated chronic HCV infection, 2/8; (f) negative HCV RNA at EOT, 4/8; (g) sustained virological response, 2/8]. Thanks to our intervention, DAA therapy was initiated in 3 out of 5 patients with an untreated chronic HCV infection, and in one patient, an SVR was already documented. Also, one patient with a negative EOT PCR already achieved SVR. Within one year, we will re-assess LTFU rates in the 45 remaining patients and hopefully re-introduce the majority of them into the care continuum.
Conclusions: LTFU rates in the GP/primary care patient population are similar to the LTFU rates observed in the secondary and tertiary care patient population in Belgium. Again, half of patients who dropped out, were successfully reintroduced in the hepatitis C care cascade. Given that the lost-to-follow-up strategy comes without screening costs, this is a feasible and highly cost-effective strategy on the road towards HCV elimination.

- B01 -

A DUAL FIELD OF VIEW MULTIPHOTON MICROSCOPE TO INVESTIGATE CONNECTIONS AND CONNECTIVITY IN THE ENTERIC NERVOUS SYSTEM. Y. Kazwiny (1), C. Fung (1), T. Martens (1), W. Boesmans (2), P. Vanden Berghe (3) / [1] KUL - University of Leuven, Leuven, Belgium, TARGID, [2] Hasselt University, Hasselt, Belgium, BIOMED, [3] KUL - University of Leuven, Leuven, Belgium, Lab. for Enteric NeuroScience (LENS), TARGID.

Introduction: Many biological processes are controlled by central and peripheral neuronal circuits that receive and integrate different input signals. Functional defects in these circuits, which can be caused by developmental errors or as a consequence of disease, can have long lasting detrimental effects ranging from unexplained pain to severe dysfunction. Most neuronal circuits have rather complex three-dimensional cellular organizations and therefore require dedicated methodology to be unraveled. The enteric nervous system, embedded in the intestinal wall, is such a typical 3D network, which consists of two main layers of neurons and glia cells that control many local functions of the gastrointestinal tract.
Aim: To establish an optical imaging platform that is capable of visualizing activity of individual neurons simultaneously at different locations in an organ.
Results: We developed a dual microscope that consists of one objective lens in an upright configuration, which can be moved in 3 directions (x, y and z). A second identical objective lens is mounted on an inverted microscopy stand, which can, similarly but independently, also be moved in the 3 dimensions. This configuration allows us to visualize two fields of view at large distances (up to tens of millimeters) simultaneously and as such enables investigating synchronized cellular activity. Excitation of fluorescent molecules can be elicited either in widefield or by non-linear multiphoton point-scanning illumination in case deep penetration in the tissue is required. Taking advantage of genetic strategies to express GCaMP Ca2+ indicators in the enteric nervous system (e.g Wnt-1 Cre x fl/fl GCaMPx), we use this dual location imaging approach to investigate the communication between the submucous and myenteric plexus' neurons, the coordination of myenteric plexus activity at locations millimeters away from each other, as well as in two locations at either side of the intestine, to probe circumferentially coordinated activity. The recordings indicate that synchronized activity occurs in coordinated bursts, both in circumferential as well as in longitudinal direction, and also in the myenteric and submucous plexus.
Conclusions: The new imaging platform will help to understand how the enteric nervous system controls intestinal behavior and allows probing the circuits and reflexes with (sub) cellular resolution. Apart from being utilized in intestinal tissues, the dual microscope concept also holds promise to optically study any type of coordinated activity in cellular networks and organisms that do not fit within one field of view at a certain magnification and resolution.

- B02 -

STUDY ON THE ROLE OF INTESTINAL MUSCULARIS MACROPHAGES IN DIABETIC NEURODEGENERATION. M. Vandeput (1), M. Chavero-Pieres (1), N. Stakenborg (1), Z. Wang (1), I. Appeltans (1), M. Francesca Viola (1), M. Delfini (1), G. Boeckxstaens (1) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Chronic diseases and Metabolism (ChroMeta).

Introduction: Gastrointestinal dysfunction related to neurodegeneration is a major complication of long-term poorly controlled diabetes. In particular, delayed gastric emptying or gastroparesis and other gastrointestinal complaints such as constipation or diarrhoea are commonly reported in diabetes. Muscularis macrophages (MMϕ) are located in close proximity to enteric neurons in the myenteric plexus and are critical for neuronal function and survival. Notably, using scRNAseq, we recently identified a MMϕ subpopulation, referred to as neuron-associated MMϕ (NA-MMϕ), that can be identified by the expression of the tight junction protein F11r (CD321). This NA-MMϕ population resides in close association with neuronal cell bodies and neuronal fibers, while loss or dedifferentiation of this population results in a reduction of enteric neurons in the small intestine of adult mice (Viola et al., 2023), suggesting a crucial role of NA-MMϕ in the maintenance of the enteric nervous system.
Aim: Here, we hypothesized that gastrointestinal dysfunction in diabetes results from changes in phenotype and/or function of MMϕ, in particular of the NA-MMϕ population, leading to neurodegeneration.
Methods: Diabetes was induced in 10-week old C57/BL6J mice by intraperitoneal injection of streptozotocin (50mg/kg). Gastric emptying was measured using MRI at t=60min after feeding of a standardised 0.2g meal as previously described (Chavero-Pieres and Viola et al., 2022) at week 14, 15 and 16 after disease induction. Colonic transit was measured by placing a 3mm glass bead 2cm into the colon, and distal colonic transit time was assessed by measuring the amount of time between bead placement and expulsion of the bead. The normal ranges for gastric emptying and colonic transit were defined by the 95th percentile set by non-diabetic controls. Animals displaying values above this threshold were classified as delayed. Enteric neurodegeneration was assessed by immunohistochemical quantification of HuC/D+ somata in the myenteric plexus of the distal stomach and distal colon. Gastric and colonic single cells in the muscularis externa were isolated and stained for flow cytometry. NA-MMϕ were identified as CD45+CD11b+CD64+CD163-CD321+ cells

Results: In diabetic mice with delayed gastric emptying, but not in those with normal gastric emptying, the number of myenteric neurons was significantly decreased compared to controls (control: 602 ± 63 neurons/mm2, n=5 vs diabetic normal emptying: 537 ± 118 neurons/mm2, n = 10; p =0.450; vs diabetic delayed emptying: 454 ± 72 neurons/mm2, n=7; p = 0.040). Similarly, there was a significant loss of myenteric neurons in the colon of diabetic mice compared to controls (control: 523 ± 65 neurons/mm2, n=4 vs diabetic: 384 ± 51 neurons/mm2, n=10; p=0.001). Of interest, there was a significant reduction in the percentage of NA-MMϕ in the stomach (control: 15.1 ± 2.2 %, n=10 vs diabetic: 11.2 ± 3.2 % of CD64+ MMϕ, n=12, p=0.004) and a trend towards a reduced frequency of NA-MMϕ in the colon compared to controls (control: 7.5 ± 2.0 %, n=11 vs diabetic: 6.1 ± 1.3 % of CD64+ MMϕ, n=12; p=0.056). Of note, a stronger reduction in NA-MMϕ was observed in the colon of mice with a delayed colonic transit compared to controls or diabetic mice with a normal colonic transit (control: 7.5 ± 2 % of CD64+ MMϕ, n=11 vs diabetic normal colonic transit: 6.6 ± 1.5 % of CD64+ MMϕ, n=7, p =0.537; vs diabetic delayed colonic transit: 5.3 ± 0.8 % of CD64+ MMϕ; n=5, p = 0.056).
Conclusions: Our results indicate that diabetes leads to a reduction in the proportion of NA-MMϕ in both the gastric and colonic muscularis externa, which is more pronounced in animals that develop delayed colonic transit. The reduction of NA-MMϕ is associated with a reduction in myenteric neurons, resulting in delayed gastric emptying and constipation. Taken together, these data suggest a role for NA-MMϕ in diabetic intestinal neurodegeneration. Further studies identifying the transcriptional changes and pathways involved may ultimately lead to the identification of novel therapeutic targets.

- B03 -

MUCOSAL ENTERIC GLIA COLONIZE THE LAMINA PROPRIA INDEPENDENT OF VAGAL INNERVATION. G. Sanchini (1), C. Cirillo (2), H. Enomoto (3), W. Boesmans (1) / [1] Hasselt University, Hasselt, Belgium, Health and Life Science, [2] INSERM, France, Toulouse NeuroImaging Centre (ToNIC - UMR1214 Inserm/UT3), [3] Graduate School of Medicine, Kobe University, Kobe, Japan, Department of Physiology and Cell Biology, Division of Neural Differentiation and Regeneration.

Introduction: Mucosal enteric glia are a sub-population of enteric glia residing in the intestinal lamina propria. These enteric glial cells characterized by type-III morphology have been implicated in the regulation of intestinal barrier function and maintenance of epithelial stem cells. Previously, it has been shown that germ-free mice present with a reduced density of mucosal enteric glia. After conventionalization and restoration of the intestinal microbiome, the population of mucosal enteric glia is re-established by enteric glia originating from the myenteric plexus. This migratory capacity is preserved in physiological conditions and reflects the ordered colonization of the serosa-mucosa axis by ENS progenitors during development.
Aim: The mechanisms that govern the migration and positioning of enteric glia in the mucosa remain obscure. Because of their glial nature, we hypothesize that enteric glial cells require mucosal innervation for their migration towards the lamina propria and maintenance within intestinal villi.
Methods: The positioning and density of enteric glia were analyzed in the small intestine of Sox10-CreERT2;Ai14 reporter mice and using immunofluorescence labeling for Sox10 and S100β in whole mounts obtained from germ-free mice or after their conventionalization. In addition, the number and location of mucosal enteric glia were examined in a surgical model of unilateral sub-diaphragmatic vagotomy, which was employed to eliminate the extrinsic neuronal component of the lamina propria. vGlut-Flp;Phox2B-Cre;Ai65 mice, expressing the fluorescent reporter tdTomato in afferent fibers of the vagus nerve specifically, were used to determine the effectiveness of the surgeries and to examine the association between vagal afferents and mucosal enteric glia.
Results: In line with earlier reports, we found a reduced density (49.5%) of mucosal enteric glia in the villi of the ileum of germ-free mice, with the remainder of glia located close to the villus base. A similar result was observed in the jejunum (54.9% reduction), but not in the duodenum. Notably, the absence of microbiota was associated with an increase in villi length in the duodenum (43.0% longer) and ileum (34.3% longer), for which we corrected in our quantifications of glia density. Unilateral vagotomy did not affect mucosal or myenteric glia density in control animals, nor did it impact the colonization of the lamina propria by enteric glia induced by conventionalization of germ-free animals.
Conclusions: We provide new insights into the interaction between microbiota and mucosal enteric glia. Our results indicate that microbiota shape the architecture of the intestinal mucosa. In addition, by performing region-specific vagotomy experiments, we demonstrate that mucosal enteric glia do not require vagal innervation for their migration or presence in the lamina propria of the mouse small intestine. Our current experiments focus on the histo-spatial interactions and cellular activity patterns instructing mucosal enteric glia homeostasis.

- B04 -

ROLE OF AIRBORNE AND FOOD ANTIGEN CROSS-REACTIVITY IN THE ASSOCIATION BETWEEN ALLERGIC AIRWAY PATHOLOGY AND IRRITABLE BOWEL SYNDROME. M. Cuende Estévez (1), S. Cuypers (2), W. Backaert (2), H. Hussein (1), I. Appeltans (1), K. Bellens (1), J. Vanoirbeek (3), L. Van Gerven (2), G. Boeckxstaens (1) / [1] KUL - University of Leuven, Leuven, Belgium, Translational Research in Gastrointestinal Disorders (TARGID), [2]

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Introduction: Epidemiological studies have demonstrated the concomitance of irritable bowel syndrome (IBS) and airway diseases, such as asthma and rhinitis. Production of antigen-specific IgE and subsequent mast cell (MC) activation upon exposure to the offending antigens have been shown to play a major role in the pathophysiology of these diseases, leading respectively to abdominal pain and airway hyperreactivity. We hypothesize that molecular similarities between airborne and food antigens underlie the concomitance of IBS and allergic airway disorders, such as asthma or rhinitis. As a consequence of this molecular mimicry, the immune system will mount a response and develop antibodies that will recognize both the food and the airborne antigens, a phenomenon known as cross-reactivity. We propose that allergy in the airways triggers sensitization of intestinal MC, followed by intestinal MC degranulation, and afferent neuron sensitization upon exposure to dietary antigens with similar a molecular structure as the sensitizing aeroallergen, ultimately leading to the concomitant development of an allergic airway disease and IBS.
Aim: In this study we aim to evaluate the role of lung and gut cross-sensitization and antigen cross-reactivity between airborne and dietary antigens as a common disease mechanism in the concomitant development of allergic airway diseases and IBS.
Methods: Patients with allergic upper airway pathology (AUAP, n=109; allergic rhinitis with/without concomitant non-allergic rhinitis (NAR) or chronic rhinosinusitis (CRS)), non-allergic upper airway pathology (N-AUAP, n=96; NAR and CRS) and healthy volunteers (HV, n=44) participated in a questionnaire-based case-control study where the prevalence of IBS and food-induced abdominal symptoms was evaluated. Dietary triggers for abdominal symptoms were subdivided into fruits/nuts (type 1), tomato/melon (2), shellfish (3), dairy products (4), FODMAPs (5) or gluten (6). Results are shown as odds ratio (OR, 95% CI) and prevalence (%, 95% CI). In parallel, mice were subjected to repeated endonasal administration of ovalbumin (OVA) +/- Staphylococcal enterotoxin B (SEB) before being orally re-exposed to OVA or saline. Airway hyperreactivity (AHR), measured as airway resistance to increasing doses of methacholine, was used as read-out for airway sensitization. Visceromotor response to colorectal distention was used as a proxy for visceral pain.
Results: Using Rome IV criteria, we observed an increased OR of IBS in patients with AUAP and N-AUAP compared to HV (AUAP: 1.55, 0.58-4.08; N-AUAP: 2.20, 0.17-5.73; HV: 0.65, 0.25-1.73, p=0.141), although this was not statistically significant. Although all groups reported general GI symptoms evoked by at least one food type, food types 1, 2, and 3 evoked abdominal pain in AUAP (6%, 5% and 2%, respectively) and N-AUAP (14%, 7% and 5%, respectively), but not in HV. In mice, nasal application of SEB/OVA resulted in the development of AHR in 41% of mice (n=9). Interestingly, after oral gavage of OVA, 78% of mice exposed to nasal SEB/OVA, but not mice exposed to nasal OVA (n=8) or SEB alone (n=9), developed VHS.
Conclusions: Our clinical and pre-clinical data show a privileged link between upper airway disorders and IBS, suggesting a crosstalk between the airway and intestinal mucosal immune system. Increased prevalence of GI symptoms towards cross-reactive foods in patients with AUAP may potentially explain the association between upper airway disorders and IBS.

- B05 -

INTESTINAL PERMEABILITY IN IRRITABLE BOWEL SYNDROME (IBS) AND IBS COMORBID: RESULTS FROM DISCOVERIE PROJECT.

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Introduction: Irritable bowel syndrome (IBS) is a disorder of brain-gut interaction (DBGI) often accompanied by psychiatric and/or somatic comorbidities. Intestinal permeability (IP) has long been hypothesised to be a key player in IBS pathophysiology. Intestinal permeability may be related to low-grade inflammation and lead to uncontrolled permeation of molecules and gut microbiota, thus disrupting the communication with the brain and other organs, eventually causing GI symptoms and psychiatric/somatic comorbidities. Studies assessing the IP in IBS using in vivo sugar excretion tests show discrepant results and are mainly using small cohorts of subjects recruited in a single centre.
Aim: This study assessed the IP in a large multicentric cohort of adult IBS patients with and without psychiatric/somatic comorbidities.
Methods: IBS patients with (N=163, age (46 (19-74) years, 87% females) and without (N=134, age (40 (20-79) years, 73% females) comorbidities fulfilling Rome IV criteria were included in five European hospitals in Belgium, The Netherlands, Sweden, Spain, and Italy. Subjects with no signs of GI disease were used as controls (N=23, 26 (20-61) years, 65% females). Intestinal permeability was assessed both in vivo with the lactulose-mannitol-sucralose test and ex vivo in colonic biopsies studied in Ussing chambers. Concentrations of the sugars in urine were measured using GC-MS in a single centre. The lactulose/mannitol (L/M) ratio after 2 hours was used to estimate the small intestinal permeability, the percentage of sucralose (%S) excreted and the sucralose/mannitol (S/M) ratio during 2-24 hours were used to assess colonic permeability. Colonic biopsies were collected from 17 controls and 18 IBS patients and mounted in Ussing chambers to measure the paracellular permeability to FITC-dextran (4 kDa).

Results: L/M ratio did not differ in IBS patients with (0,0158 (0,003-0,093), p=0,36) and without comorbidities (0,0163 (0,005-0,069) p=0,74) when compared with controls (0,018 (0,009-0,053)). Moreover, the %S excreted was not different in IBS patients with (1,057 (0,24-4,081), p=0,18) and without (0,95 (0,217-4,643), p=0,07) comorbidities when compared to controls (1,289 (0,451-2,53). Similarly, the S/M ratio was not different in IBS patients with (0,045 (0,0069-0,9), p=0,13) and without comorbidities (0,045 (0,007-0,8), p=0,18). No differences were observed comparing the three experimental groups within each hospital separately. Interestingly, when comparing results from overall IBS patients among hospitals, strongly significant differences were found in L/M ratio (p<0,0001), %S (p<0,0001), and S/M ratio (p<0,0001). Lastly, paracellular permeability assessed ex vivo in colonic biopsies was not different between IBS patients (47,9 ± 4,1 pmols, p=0,46) and controls (43,67± 4,1 pmols).
Conclusions: Taken together these results suggest that IBS patients with and without comorbidities have an unaltered small intestinal and colonic permeability. However, our results suggest a strong variability between IBS patients of different countries, which may be explained by life-style, environmental, and genetic factors. Further investigations are needed to better understand these findings.

- B06 -

TREATMENT WITH THE HISTAMINE 1 RECEPTOR ANTAGONIST EBASTINE FOR NON-CONSTIPATED IRRITABLE BOWEL SYNDROME: A DOUBLE-BLIND RANDOMIZED PLACEBO-CONTROLLED TRIAL. F. Pia (1), L. Decraecker (1), D. De Looze (2), D. Hirsch (3), H. De Schepper (4), J. Arts (5), P. Caenepeel (6), A. Bredenoord (7), T. Vanuytsel (1), A. Belmans (8), G. Boeckxstaens (1) / [1] KUL - University of Leuven, Leuven, Belgium, Translational Research in GastroIntestinal Disorders, [2] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology, [3] Pathology-DNA Rijnstate Hospital Arnhem, Arnhem, The Netherlands, Department of Gastroenterology and Hepatology, [4] Antwerp University Hospital, Edegem, Belgium, Department of Gastroenterology and Hepatology, [5] AZ Sint-Lucas Brugge, Assebroek/ Brugge, Belgium, Department of Gastroenterology, [6] Ziekenhuis Oost Limbug (ZOL), Genk, Belgium, Department of Gastroenterology and Hepatology, [7] Amsterdam UMC, Amsterdam, The Netherlands, Department of Gastroenterology and Hepatology, [8] KUL - University of Leuven, Leuven, Belgium, Interuniversity Centre for Biostatistics and Statistical Bioinformatics.

Introduction: Abdominal pain is a hallmark symptom of irritable bowel syndrome (IBS). One of the mechanisms contributing to increased abdominal pain is visceral hypersensitivity (VHS), defined as enhanced perception to stimuli, resulting from histamine 1 receptor mediated sensitization of visceral nociceptors. In a pilot study, we showed that treatment of IBS patients with ebastine, a second-generation histamine 1 receptor-antagonist, increased symptom relief and reduced abdominal pain.
Aim: To further confirm these findings, we designed a phase IIb placebo-controlled randomized multicentre clinical trial evaluating the effect of a 12-week ebastine treatment in non-constipated IBS.
Methods: 202 patients (mean age 32±11 years, 68% female) fulfilling the Rome III criteria were randomly assigned to receive 20mg ebastine or placebo once daily for 12 weeks, of which 177 completed the study. Subjects scored global symptom relief (GSR, 7-point Likert scale, weekly), abdominal pain (AP, VAS scale, daily) and number of loose stools (type 6-7 Bristol Stool Scale, daily). A subject is considered a weekly responder for GSR if total or obvious relief is experienced and a responder for AP if the weekly average pain score is reduced by at least 30% versus baseline. Primary endpoints according to FDA and EMA guidelines: weekly responders for GSR and AP combined (GSR+AP, FDA), and for GSR and AP separately (EMA), for at least 6 out of 12 treatment weeks. Secondary endpoints and post-hoc efficacy outcomes include the effect on stool consistency for patients with diarrhea-predominant IBS (IBS-D), and the proportion of weekly GSR+AP responders for 3 of the last 6 treatment weeks. In addition, the Hospital Anxiety and Depression Scale (HADS), Patient Health Questionnaires (PHQ) and Quality of Life (SF36) were evaluated at baseline and after 12 weeks.
Results: Treatment with ebastine resulted in significantly more responders (12%) for GSR+AP compared to placebo (4%, p=0.047, primary FDA endpoint) while the proportion of responders for GSR and AP separately was higher for ebastine, albeit not statistically significant (ebastine vs placbeo, GSR: 15% vs 7%, p=0.072; AP: 37% vs 25%, p=0.081, primary EMA endpoints). The effect of ebastine was slow in onset reaching a plateau from week 6 onwards leading to higher responder rates in the last 6 weeks of treatment. Analysis of the responder rate during the last 6 weeks confirmed the superiority of ebastine compared to placebo: GSR+AP, 19% vs 8%, p=0.04; GSR, 20% vs 13%, p=0.17; AP, 49% vs 34%, p=0.04 respectively. Moreover, ebastine had a significantly greater effect on the decrease in weekly abdominal pain scores during the treatment period compared to placebo (p=0.037). The percentage of stool consistency and AP responders for at least 6 out of the 12 treatment weeks in IBS-D patients was higher with ebastine compared to placebo, although not statistically significant (ebastine vs placebo, 15% vs 7%, p=0.131). No differences in HADS, PHQ or SF36 scores were detected between the ebastine and placebo groups after 12 weeks.
Conclusions: Our study shows that 12-week treatment with 20 mg ebastine is superior to placebo suggesting that histamine 1 receptor antagonism is a novel treatment for non-constipated IBS.

- B07 -

PSYCHOLOGICAL SYMPTOMS BUT NOT INFLAMMATORY PARAMETERS DIFFERENTIATE BETWEEN FUNCTIONAL DYSPEPSIA WITH OR WITHOUT OVERLAPPING IRRITABLE BOWEL SYNDROME AND GASTROESOPHAGEAL REFLUX DISEASE. M. Ceulemans (1), P. Huyghe (1), L. Wauters (1), L. Van Oudenhove (1), J. Tack (1), T. Vanuytsel (1) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, ChroMeta.

Introduction: Functional dyspepsia (FD) is characterised by a high degree of overlap with other disorders of gut-brain interaction (DGBI) such as irritable bowel syndrome (IBS) and also gastroesophageal reflux disease (GERD). Although a recent large internet survey showed higher gastrointestinal (GI) and psychological symptoms with an increasing number of DGBIs (Sperber et al. Clin. Gastroenterol. Hepatol. 2022), the GI pathophysiology underlying these overlapping conditions remains unclear. Intestinal immune activation is thought to play a role in the pathogenesis of all these disorders, and we hypothesised that signs of immune activation are more pronounced with more overlapping disorders.
Aim: We aimed to confirm the previously reported increase in GI and psychological symptoms in a cohort of FD patients with and without overlapping IBS and GERD, and assess whether immune-related parameters differ between these groups. Furthermore, we aimed to explore differences in symptomatic and inflammatory parameters among FD subtypes.
Methods: Patients with predominant FD symptoms fulfilling Rome IV criteria were previously included in an interventional study and also completed psychological [anxiety (Generalised Anxiety Disorder 7, GAD-7); stress (Perceived Stress Scale, PSS); depression (Patient Health Questionnaire 9, PHQ-9)], general somatic symptoms (PHQ-12)) as well as GI-specific symptom (Patient Assessment of GI Disorders Symptom Severity Index, PAGI-SYM) questionnaires. Overlap with other GI disorders was assessed through ReQuest (GERD) and Rome IV IBS questionnaires. Patients underwent upper-GI endoscopy with collection of duodenal biopsies and duodenal fluid through a nasoduodenal catheter. Blood was drawn and high-sensitivity C-reactive protein was measured in fasting plasma samples using turbidimetry. Mucosal eosinophils and intra-epithelial lymphocytes (IEL) were counted on H&E or CD3 stained biopsy slides per mm² or per 100 enterocytes, respectively. Duodenal eosinophil-derived neurotoxin (EDN) was measured in whole-biopsy lysates and duodenal aspirates using ELISA. Symptom scores were analysed by Mann-Whitney U tests, while inflammatory parameters were log transformed and analysed by unpaired t tests, with step-down Bonferroni correction for GI-overlap analyses.
Results: In this analysis, 28 FD patients with mean age of 32 (± 12) years (86% females) were subdivided based on the presence or absence of other GI disorders: 6 had only FD, 11 had an overlap with GERD or IBS and 11 had an overlap with both. Alternatively, FD patients were categorised based on their FD subtype into 15 pure postprandial distress syndrome (PDS) patients and 13 patients with combined epigastric pain syndrome (EPS) and PDS+EPS overlap (PDS+EPS/EPS), as only 2 patients had pure EPS complaints. Age and sex distribution were similar across groups. PAGI-SYM scores tended to be higher in FD patients with IBS+GERD overlap compared to FD without overlap (2.6 vs 1.8; Padj = .080). GAD-7 (7.4 vs 0.8; Padj = .023) and PHQ-12 (12.3 vs 4.2; Padj = .015) scores were significantly higher in FD patients with IBS+GERD overlap versus without overlap, but not different from FD patients with IBS or GERD (all Padj > .1). No differences in PSS or PHQ-9 scores were seen between the overlap subgroups (all Padj > .1). All immune-related parameters – duodenal IEL counts, mucosal or luminal EDN levels and systemic hsCRP – were similar between subgroups (all Padj > .1), except for a trend towards higher duodenal eosinophil counts in the IBS+GERD overlap group versus FD with IBS or GERD (256 vs 188 /mm²; P = .096). Looking at FD subtypes, PSS (18.8 vs 10.1; P = .027) and PHQ-9 (8.5 vs 4.6; P = .032) scores were higher in the PDS+EPS/EPS group compared to pure PDS, whereas PAGI-SYM, GAD-7 and PHQ-15 scores were similar between groups (all P > .1). Interestingly, duodenal eosinophils were higher in the PDS+EPS/EPS group (249 vs 187 /mm²; P = .040) compared to pure PDS, while other inflammatory parameters were similar between groups.
Conclusions: Here, we demonstrate that FD patients with overlapping GERD and IBS reported more anxiety and general somatic symptoms compared to FD without overlap, confirming the high psychological burden of multiple overlapping GI disorders. In contrast, immune-related factors failed to differentiate between these groups. Among FD subtypes, the PDS+EPS/EPS group reported higher stress and depressive symptoms compared to pure PDS patients, and had higher duodenal eosinophil counts, which contrasts with previously reported associations between PDS symptoms and eosinophils.

- B08 -

STUDY EVALUATING THE RELATIONSHIP BETWEEN THE MICROBIOME, PROTEOLYTIC ACTIVITY, BACTERIAL SUPERANTIGENS AND CLINICAL SYMPTOMS IN PATIENTS WITH IRRITABLE BOWEL SYNDROME. R. Quan (1), H. Hussein (1), M. Cuende-Estévez (1), L. Decraecker (1), G. Boeckxstaens (1) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Aging.

Introduction: Dysbiosis has been proposed as one of the mechanisms involved in the pathogenesis of IBS. Specifically, bacterial strains associated with high proteolytic activity or histamine production have been reported to contribute to

visceral hypersensitivity. Recently, we showed that Staphylococcal enterotoxin B (SEB), a superantigen (SAg) produced by Staphylococcus aureus, is able to break oral tolerance to food antigens and trigger dietary antigen-specific IgE antibody production, subsequently leading to mast cell activation and abdominal pain following food intake. These data suggest a potential role of the microbiome in IBS, but to what extent these findings are related to clinical symptoms remains to be proven.

Aim: In this study, we aimed to confirm previously reported alterations in the abundance of bacterial strains mechanistically involved in (1) mediation of proteolytic activity, (2) histamine production, and (3) superantigen production in IBS patients and evaluate the impact on clinical symptoms.

Methods: A total of 309 fecal samples (IBS: n=218 (89 IBS-D, 46 IBS-C, 38 IBS-M, 45 IBS-U); HV: n=91) and 214 nasal swabs (IBS: n=176 (73 IBS-D, 35 IBS-C, 31 IBS-M, 37 IBS-U); HV: n=38) were collected from IBS patients and HV recruited by public advertisements. Abdominal symptoms were assessed by the IBS severity scoring system (IBS-SSS) and the visual analogue scale (VAS) for abdominal pain and bloating (ranging from 0 to 10). Whole gut transit time was assessed using the Bristol Stool Scale and a radio-opaque marker study first described by Hinton et al. The presence of SAgs (SEA, SEB, SEC, SED, SEG, SEH, SEL, SEM, SEO, SEK) and bacterial species (S.pyogenes, S.aureus, Paraprevotella clara, Alistipes putredinis, Blautia obeum, Collinsella aerofaciens, Dorea formicigenerans, Enterocloster bolteae, Bacteroides ovatus, Klebsiella aerogenes) were determined by qPCR. Trypsin-like activity in fecal supernatants was detected by measuring the fluorescence intensity using a spectrophotometer after the cleavage of a fluorogenic substrate of trypsin.

Results: The relative abundance of P.clara and A.putredinis, known to inhibit proteolytic activity, was significantly lower in fecal samples from IBS patients compared to HV, whereas B.obeum and E.bolteae were more enriched in IBS fecal samples. Using Spearman correlation analysis, a moderate negative correlation was shown between fecal trypsin-like activity and the presence of P.clara ($rs= -0.48$, $p<0.0001$) and A.putredinis ($rs= -0.43$, $p<0.0001$) in IBS patients while a weak and positive correlation was found for B.obeum ($rs= 0.29$, $p<0.01$). Moreover, A.putredinis was negatively associated with VAS pain scores of IBS patients ($rs= -0.41$, $p<0.0001$). The histamine super-producer K.aerogenes was detected in 5% of IBS and 6 % of HV ($p>0.05$). Notably, the percentage of fecal samples containing S.aureus was significantly higher in IBS compared to HV (20% compared to 9%, $p<0.05$) whereas no difference was found in nasal swabs from IBS patients (68%) compared to HV (73%). Of interest, 49% of IBS fecal samples positive for S. aureus were also positive for one or more SAgs compared to only 12% in HV. Interestingly, IBS patients with positive SAg-producing S.aureus in fecal samples had higher pain scores compared to those without (VAS score: 5.8±1.6 compared to 3.9±1.5, $p<0.05$).

Conclusions: Although several bacterial strains (P.clara, A.putredinis, B.obeum and E.bolteae) are differentially abundant in IBS and associated with altered fecal proteolytic activity, only A.putredinis, known to inhibit proteolytic activity, is inversely related to abdominal pain. The exact mechanism involved remains however to be clarified. In line with our previous preclinical study indicating a role for SAg in breaking oral tolerance and resulting in visceral hypersensitivity, we here report an increase in SAg-producing S.aureus in fecal samples of IBS patients, suggesting a potential role in the pathogenesis of a subpopulation of IBS patients.

- B09 -

MONOCYTE AND MACROPHAGE HETEROGENEITY IN THE HUMAN GUT IN HEALTH AND DISEASE.
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Introduction: Crohn's disease (CD) is characterized by recurrent inflammation of the gastrointestinal (GI) tract. It is a complex immune-mediated disease that arises in genetically susceptible individuals with a dysregulated immune response towards their microbiome and other environmental factors. A growing body of evidence postulates that monocytes and their macrophage progeny are key drivers in CD pathology. Indeed, their excessive immune response triggers chronic intestinal inflammation that provokes significant tissue damage and gut barrier dysfunction eventually causing progressive fibrosis.

Aim: To characterize monocyte and macrophage heterogeneity in human gut in health and CD

Methods: Transmural ileum tissue specimens were obtained from patients undergoing ileocolonic resection due to colorectal cancer (CRC) (n=6) or CD (n=6). The mucosa, submucosa and muscularis propria were dissected from each other and digested with Liberase to make single cell suspensions. Live monocytes and macrophages were FACS-sorted to perform single cell RNA sequencing. Raw sequencing reads were demultiplexed, mapped to the human reference genome and gene-expression matrices were calculated. After normalization, these cells were clustered using the Seurat workflow.

Results: We profiled the transcriptome of 152.426 cells following exclusion of doublets and contaminating and low quality cells. Unsupervised clustering followed by annotation of the integrated gene expression data identified the following myeloid populations: Mature Mac 1 (LYVE1, RNASE1, F13A1), Mature Mac2 (SLC40A1, SELENOP, C1QC) and

Mature Mac3 (CCL18 ,RNASE1, FOLR2). Other macrophage clusters were defined as IL4I1+ macrophages (CXCL9, CXCL10 and IDO1) and MMP9+ macrophages (TREM2, MMP9 and FABP5) and cytokine-rich Macs, as shown by their increased expression of pro-inflammatory factors (IL1RN, IL1A, EREG, CCL4L2). In addition, we describe a differentiating Mac cluster (HLA-DRB5, CXCR4, S100A10), a classical monocyte cluster (S100A12, VCAN, FCN), a cytokine-rich monocyte cluster (S100A12, VCAN, TNF) and CD1c+ DC cluster (CD1C, CLEC10A, FCER1A). High-resolution characterization of the different monocytes, cDC1+ DC and macrophages revealed major reorganization in the myeloid compartment between inflamed and uninflamed ileum. We found that classical and cytokine-rich monocytes were highly enriched in the CD mucosa, while all mature Macs were severely decreased in the mucosal layer of CD patients compared to CRC controls. In the CD submucosal and muscularis propria layer, the influx of monocytes and reduction of mature Macs was less evident. Interestingly, the inflamed CD tissue was enriched for 2 macrophage clusters, i.e. MMP9+ and IL4L1+ macrophages, of which IL4I1+ Macs were found in all intestinal layers, while MMP9+ Macs were mainly enriched in submucosal and muscularis externa layer of the gut. Given the strong expansion of MMP9+ macrophages in CD ileum, we sought to functionally characterize them. This Mac subset possessed a transcriptional signature of Mmp9, Lipa, Lpl, Fabp5, Lgals3, genes associated with lipid metabolism and tissue remodeling. Notably, the MMP9+ gene signature was shown to be highly conserved in disorders with a strong accumulation of lipids (i.e. obesity, fatty liver) and development of organ fibrosis (i.e. lung, liver, kidney and heart) in both mouse and human. Next, we ranked all genes by their relative enrichment, followed by functional classification of the most characteristic genes according to GO term pathway analysis. This approach revealed a strong enrichment of MMP9+-expressed genes in pathways related to phago- and endocytosis as well as lipid metabolism and tissue remodeling. Trajectory analysis further showed that MMP9+ Macs appear to have a monocytic origin. Besides the MMP9+ macrophages, we also identified IL4I1+ macrophages in the CD ileum. This Mac subset possessed a transcriptional signature of Cxcl9, Cxcl10, Ido1, genes associated with immune regulation and interferon-gamma signaling, which was confirmed by GO term analysis. Trajectory analysis further showed that IL4I1+ Macs also appear to have a monocytic origin.
Conclusions: We identified two understudied macrophage populations that were highly specific to the inflamed CD gut, i.e. MMP9+ and IL4I1+ Macs. The MMP9+ Macs have been associated with deregulated lipid metabolism and fibrosis, while the IL4I1+ Macs have shown to regulate immune response. Their function in CD remains to be further studied.

- B10 -

AN ANTI-FIBROTIC ROLE FOR EOSINOPHILS IN A DSS COLITIS RAG-/- AND AN IN VITRO CO-CULTURE MODEL. I. Jacobs (1), S. Deleu (2), J. Cremer (3), E. Dilissen (3), G. De Hertogh (4), T. Martens (5), P. Vanden Berghe (5), S. Vermeire (6), C. Breynaert (7), T. Vanuytsel (6), B. Verstockt (6) / [1] KUL - University of Leuven, Leuven, Belgium, Department microbiology, immunology and transplantation, [2] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism, Translational Research Center for Gastrointestinal Disorders (TARGID), [3] KUL - University of Leuven, Leuven, Belgium, Department of Microbiology, Immunology and Transplantation, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Imaging and Pathology, Translational Cell & Tissue Research, [5] KUL - University of Leuven, Leuven, Belgium, Cell and tissue Imaging Core, [6] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [7] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of General Internal Medicine.

Introduction: In several disease areas, such as in the liver and lungs, a pro-fibrotic role for eosinophils has been suggested. However, information about the role of eosinophils in the development of intestinal fibrosis is scarce.
Aim: We therefore aimed to assess the functional and mechanistic role of eosinophils in intestinal fibrosis and fibroblast activation.
Methods: Chronic DSS colitis (3 DSS cycles of 1 week DSS administration followed by 2 weeks of recovery (1.75% - 2.25% - 2.25%)) was introduced in 6-8-week-old C57BL/6 RAG-/- mice to induce intestinal fibrosis. Mice were injected intraperitoneally with anti-CCR3 to deplete eosinophils (n=8) or with an isotype control (n=8). Intestinal fibrosis was assessed based on collagen deposition (hydroxyproline assay, Martius Scarlet Blue staining (MSB) and second harmonics generation (SHG)), while COL1A1 expression was assessed via RT-qPCR. Gene expression was performed using RT-qPCR and protein expression via the MSD platform. Secondly, circulating eosinophils were isolated from non-IBD controls (n=3) and co-cultured with fibroblasts, isolated from resection specimens obtained from the terminal ileum of Crohn's disease patients undergoing right hemicolectomy (n=3). The effect of eosinophils on fibroblast activation was assessed through the expression of α-SMA via flow cytometry and immunocytochemistry. Lastly, fibroblasts were stimulated with 10ng/mL eosinophil cationic protein (ECP), a protein exclusively produced by eosinophils (n=3), in order to study whether this mediator could affect fibroblast activation.
Results: Anti-CCR3 mediated eosinophil depletion in the chronic DSS model resulted in increased fibrosis based on the hydroxyproline assay ($p=0.06$), MSB ($p=0.005$) and COL1A1 expression ($p=0.03$). Similarly, we identified an increased collagen deposition in the eosinophil-depleted group based on the SHG. Furthermore, an increase in the pro-fibrotic IL-1β and TGF-β3 on protein ($p=0.03$ and $p=0.06$) and gene level ($p=0.04$ and $p=0.005$) could be found in the eosinophil depleted mice. Co-culturing eosinophils with fibroblasts resulted in decreased α-SMA expression, indicative of a decrease

in active fibroblasts. This could be observed via both flow cytometry (p=0.001) and immunocytochemistry. Similarly, when fibroblasts were stimulated with ECP, a decrease in α-SMA was observed (p=0.04).
Conclusions: Depletion of eosinophils in a chronic DSS RAG-/- model resulted in more intestinal fibrosis. Similarly, in an in vitro setting, eosinophils, as well as ECP, decreased α-SMA expression in fibroblasts, suggesting that eosinophils may inactivate fibroblasts.

- B11 -

THE ROLE OF MUC13 IN GASTRIC CANCER CELL DEATH INHIBITION AND DYSBIOSIS. B. Oosterlinck (1), W. Arras (1), J. G. De Man (1), B.Y. De Winter (1), A. Smet (1) / [1] University of Antwerp, Antwerp, Belgium, LEMP.

Introduction: One of the hallmark features of gastric adenocarcinomas is aberrant mucin expression which drives tumorigenesis by influencing cellular growth and survival and has been linked to initiation, progression and poor prognosis. In gastric cancer, MUC13 is overexpressed in 64.9% of cases and has been associated with worse patient survival and enrichment of oral pathogens. However, how MUC13 affects cell death signaling in the gastric carcinogenesis process remains unknown.
Aim: Here, we aimed to identify whether MUC13 is involved in tumour cell death resistance in gastric cancer and unravel the signalling pathways involved.
Methods: MKN-7 gastric cancer cells, incubated at 37°C and 5% CO2 in RPMI-1640 medium till 70% confluency, were transfected with Silencer Select MUC13 and Negative Control siRNA (control siRNA, Invitrogen) using RNAiMAX lipofectamine reagent (Invitrogen) according to manufacturer's instructions. Forty-eight hours post-transfection, cells were stimulated with either TNF-a or IL-1B at 0, 60 or 80 ng/mL. Twenty-four hours post-treatment, an MTT-cell survival assay was performed to assess cell survival through measurement of optical density and RNA extracted for bulk RNA sequencing (150bp paired end) to analyse differential gene expression and gene set enrichment.
Results: In the absence of cytokine treatment, knock down of MUC13 expression resulted in significant increased cell survival compared to control siRNA transfected cells (N= 64, P<10-5, t-test). When treated with 60 ng/mL cytokine, no significant difference in cell survival was observed between MUC13 knock-down and control cells for IL-1β while for TNF-α treated MUC13 knock-down cells survival was significantly increased (N=32, P= 0.01). In case of 80 ng/mL cytokine treatment, control cells have a significantly increased cell survival compared to MUC13 knock-down cells with a greater effect for TNF-α (N=32, P=0.0046) compared to IL-1β (N=32, P=0.047). These results are being confirmed in an in vivo gastric cancer mouse model in which female MUC13-/- or wild type litter mates were orally infected with Helicobacter pylori (SS1), H. felis (CS1) or given trypticase broth as control. After a two-week recovery period, infected animals received drinking water supplemented with 240 ppm N-Methyl-N-nitrosourea (MNU) on alternating weeks for 5 weeks. Twenty-six weeks after MNU treatment the mice were sacrificed, and the stomach (corpus & antrum) sampled for transcriptome analysis in addition to microscopic analysis of inflammation through immunohistochemistry. Transcriptome analysis is currently being performed on siRNA transfected MKN7 cells and gastric tissue samples from the Helicobacter/MNU-treated gastric cancer mouse model. Analysis of the RNA sequencing data is currently ongoing.
Conclusions: Our results emphasize a key role of MUC13 in promoting tumour cell survival in gastric cancer.

- B12 -

CHARACTERIZATION OF THE IMPACT OF NKCC1 IN COLORECTAL CARCINOGENESIS. P. Adam (1), C. Salée (2), M. Stepniak (3), J. Loly (4), S. Vieujean (4), S. Kropp (4), C. Reenaers (5), F. Fonzé (6), C. Massot (6), N. Blétard (7), C. Coimbra Marques (5), E. Decker (5), P. Delvenne (7), E. Louis (4), M. Meuwis (8) / [1] University of Liege, Liège, Belgium, Translational Gastroenterology Laboratory, [2] ULiège, Belgium, Laboratory of Translational Gastroenterology, GIGA institute, [3] ULiège, Belgium, Laboratory of Translational Gastroenterology, GIGA institute Uliège, [4] CHU de Liège, Liège, Belgium, Hepato-Gastroenterology and Digestive Oncology, [5] CHU de Liège, Liège, Belgium, Abdominal Surgery Department, [6] ULiège, Belgium, Laboratory of Translational Gastroenterology, [7] CHU de Liège, Liège, Belgium, Pathological Anatomy and Cytology, [8] CHU de Liège, Liège, Belgium, Laboratory of Translational Gastroenterology.

Introduction: Colorectal cancer associated with inflammatory bowel disease also known as colitis-associated cancer (CAC) is considered as a separate entity from sporadic colorectal cancer (CRC). Previous studies demonstrated that Solute carrier family 12 member 2 (SLC12A2/NKCC1) is a protein overexpressed in pre-tumoral and tumoral lesions of CAC and CRC. This Na-K-Cl cotransporter localized at the cell membrane and in the cytoplasm is mainly expressed in cells involved in fluid secretion and in intestinal stem cells. NKCC1 have been reported to be activated during oxidative stress which is recognized to be a major player in carcinogenesis in CRC and CAC, inducing enhanced cell proliferation and DNA damages. Despite NKCC1 up-regulation and change of distribution within dysplastic and colorectal cancers tissues, little is known about its impact and role in colorectal carcinogenesis in relation to oxidative stress.
Aim: The aim of this study is to investigate the impact of NKCC1 in colorectal carcinogenesis and more precisely its role in the regulation of oxidative stress in tumor cells.

Methods: Oxidative stress was induced on 3 different CRC cell lines (Caco-2, HT-29, HCT116) by adding H202 or by UV irradiation. Concurrently, cells were incubated with NKCC1's chemical inhibitor, bumetanide (BMT), or by NKCC1 Silencing (siRNA). Viability of cells was measured using Cell titer glo 2.0 kit (Promega). In addition, characterization of protein of Endoplasmic Reticulum (ER) stress (BiP), mTORC1 signaling (p70 S6 kinase and its phosphorylated form), apoptosis (caspase3 cleaved form) and β-catenin were monitored by Western blot.
Results: Caco-2 cells subjected to 24-hour exposure at 1 mM H2O2 and 200 µM bumetanide showed 68% to 18% decreased viability without and with BMT respectively, while HT29 viability decreased from 62% to 36% respectively. HCT116 viability dropped from 12% to 5% with BMT treatment. The loss of viability was demonstrated to be BMT concentration-dependent in Caco-2. This effect was observed exclusively under induced oxidative stress. Western blot analyses performed when using H2O2 and BMT co-treatment revealed the activation of the mTORC1 pathway and an ER stress increase. Upon specific NKCC1 silencing, a significant decrease in mTORC1 pathway activity was observed with a marked increase in the cleaved form of Caspase 3 and a strong reduction of β-catenin signal.
Conclusions: The inhibition of the catalytic site of NKCC1 led to a decrease in the viability of the 3 colorectal cell lines tested when exposed to oxidative stress. At the molecular level, we found an enhanced activation of the mTORC1 pathway, together with an increase in endoplasmic reticulum stress. When NKCC1 expression was silenced, apoptosis event could be detected, as well as the dysregulation of both the mTORC1 pathway and β-catenin. Collectively, these results suggest the importance of NKCC1 expression and activity as a Na-K-Cl cotransporter, in survival and proliferation of CRC tumors cells. The characterization of the impact of NKCC1 in carcinogenesis is currently under investigation using the 3D-organoid model derived from colorectal cancer surgical margins, from ulcerative colitis patients and using tumoroids.

- B13 -

STUDY EVALUATING THE ROLE OF BLOOD-VESSEL ASSOCIATED MACROPHAGES IN THE GUT-VASCULAR BARRIER. N. Pajk (1), M. Logist (1), M. Viola (1), N. Stakenborg (1), I. Appeltans (1), Z. Wang (1), G. Boeckxstaens (1) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing.

Introduction: In contrast to the general idea that intestinal ResMacs are short-lived and are continuously replaced by incoming monocytes, our group recently identified long-lived self-maintaining gut macrophages adjacent to submucosal blood vessels (blood vessel-associated or BVA-ResMacs) and enteric neurons of the muscularis externa (neuron-associated or NA-ResMacs). Depletion of BVA-ResMacs in the small intestine disrupts blood vessel morphology and leads to vascular leakage of microspheres into the submucosa. However, whether BVA-ResMacs are important in preventing bacterial translocation into the systemic circulation, a role previously attributed to blood endothelial cells, has not been explored yet.
Aim: To explore the role of colonic BVA-ResMacs in maintaining the gut-vascular barrier in homeostasis.
Methods: First, the intimate relationship between the vasculature and BVA-ResMacs was evaluated by microscopy in CX3CR1-Cre(ER)T2 x Rosa-LsL-YFP mice. Colonic tissue was collected 8 weeks post tamoxifen (TAM) injection, with only long-lived ResMacs maintaining the CX3CR1-YFP expression. The tissue was used for immunohistochemical staining to visualize the position of the long-lived ResMacs relative to submucosal and mucosal blood vessels (identified using CD31 and VE-Cadherin antibodies). Next, to study the role of intestinal macrophages in the gut-vascular barrier, 8 weeks old C57BL/6 mice received two doses of αCSF1r antibody (37,5µg/g BW) or IgG control via IP injection three days apart. Seven days post first IP injection, mice were anaesthetized and a >1-cm-long colonic loop was made by a double ligation of the colon without disrupting the blood flow. Fluorescent Escherichia coli (E.coli) (K-12 strain) bioparticles conjugated with Alexa Fluor 488 were injected into the colonic loop. Blood was collected by cardiac puncture 20min post injection. Translocated bacterial particles were quantified by measuring optical density of the fluorescent signal in plasma. In addition, liver tissue was isolated and embedded in OCT. Slices of 10 µm were imaged for the presence of E.coli. To evaluate the role of long-lived BVA-ResMacs, 4 weeks old CX3XR1-Cre(ER)T2 x Rosa26-iDTR pups were injected with TAM to induce diphtheria toxin receptor (DTR) expression in CX3CR1+ macrophages. At 12 weeks of age, mice received diphtheria toxin (DTx) injections (200ng / 30g BW) every other day for 2 weeks to deplete long-lived ResMacs, or saline. Fourteen days post first DTx injection, colonic loop experiment was performed as described above. In addition, colonic lamina propria was isolated and stained for DTR, macrophage-specific Iba-1 marker and blood vessel-specific CD31 marker to validate successful depletion of BVA-ResMacs.
Results: First, using CX3CR1-Cre(ER)T2 x Rosa-LsL-YFP mice, we evaluated the localization of long-lived colonic BVA-ResMacs relative to submucosal blood vessels by microscopy. CX3CR1-YFP+ ResMacs were found across the lining of submucosal blood vessels, confirming their close interaction. Depletion of macrophages with αCSF-1R antibody resulted in significantly higher content of fluorescein in plasma compared to mice that received IgG control (p-value=0.0079). In contrast, fluorescent E.coli particles were not detected in the liver. Two weeks after TAM treatment of CX3XR1-Cre(ER)T2 x Rosa26-iDTR mice, expression of DTR was confirmed to be specifically localized on CX3CR1+ macrophages, while the treatment with DT resulted in complete depletion of DTR+ macrophages at day 2 post last DT

injection. The mice devoid of long-lived ResMacs displayed significantly higher content of fluorescein in their plasma compared to saline-treated mice (p-value=0.0127).
Conclusions: Our finding sets colonic BVA-Macs as key players in maintaining the gut-vascular barrier in homeostasis. Here we demonstrate that the depletion of colonic BVA-ResMacs not only results in local leakage into the tissue, but also allows passage in the opposite direction with entrance of bacteria into the portal and systemic circulation. However, bacteria does not spread to other organs such as liver. This finding challenges the idea that the gut-vascular barrier is solely controlled by blood endothelial cells.

- B14 -

PSEUDO-ALLERGIC, MRGPRB2-DEPENDENT MAST CELL ACTIVATION PLAYS A CRUCIAL ROLE IN ACUTE COLITIS. L. Lambeets (1), S. Van Remoortel (2), J. De Man (3), B. De Winter (3), S. Martinez Ibiza (1), J. Timmermans (1) / [1] Universiteit Antwerpen / Antwerp University Hospital, WILRIJK (Antwerpen), Belgium, Laboratory of Cell Biology & Histology (CBH), [2] KUL - University of Leuven, Leuven, Belgium, Translational Research Center for Gastrointestinal Disorders (TARGID), [3] Universiteit Antwerpen / Antwerp University Hospital, WILRIJK (Antwerpen), Belgium, Translational Research in Immunology and Inflammation.

Introduction: Mast cells (MCs) are strategically positioned in the gastrointestinal mucosa to promptly respond to potential threats or damage and hence play a critical role in gut immunity and inflammation. In addition to the conventional IgE-FcεRI crosslinking, MCs can also be activated directly, without IgE involvement, to a wide range of cationic substances, including antimicrobial peptides and inflammatory (neuro)peptides. Over the past years, signaling through the Mas-related G protein-coupled receptor b2, Mrgprb2, in mice and its orthologue MRGPRX2 in humans has gained a lot of interest as an alternative MC activation pathway. Since their discovery, Mrgprb2/MRGPRX2 have emerged as important mediators driving immediate drug hypersensitivity, chronic itch conditions, antibacterial immunity and neurogenic inflammation and pain. Such broad involvement confirms the essential role of Mrgprb2 in maintaining mucosal homeostasis in the skin and underlines their high therapeutic potential. Remarkably, whereas most studies have focused on the role of Mrgprb2/MRGPRX2 in skin MCs, little is known on the relevance of this pathway in gut-residing MCs.
Aim: The aim of this study was to explore the relevance of IgE-independent, Mrgprb2-mediated signaling in colonic MCs in the healthy and acutely inflamed mouse colon.
Methods: Mrgprb2 expression and functionality were studied using a genetic labeling strategy combined with advanced microscopic imaging. Furthermore, Mrgprb2 knockout (Mrgprb2-/-) mice were used to determine the role of this pathway in a preclinical dextran sodium sulphate (DSS) colitis model.
Results: In the colon of healthy Mrgprb2-cre:tdTomato mice, we observed tdTomato+ cells that co-labeled with established connective tissue MC markers. These Mrgprb2-expressing MCs 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 MC degranulation and mediator release. Acute DSS colitis led to a pronounced increase in Mrgprb2-expressing MCs, as evidenced by an increased Mrgprb2 mRNA expression and concomitant increases in Mrgprb2-expressing MCs. Loss of Mrgprb2- mediated signaling impaired DSS-induced neutrophil influx and significantly impacted on acute colitis progression.
Conclusions: Our findings uncover a novel, IgE-independent MC degranulation pathway in the mouse colon that plays a central role in acute colitis pathophysiology, mainly by safeguarding acute colitis progression and severity in mice.

- B15 -

UNVEILING THE RELATIONSHIP BETWEEN NERVE-ASSOCIATED MACROPHAGES AND NERVES ACROSS DIFFERENT ORGANS. Z. Wang (1), N. Stakenborg (1), M. Viola (1), S. Van Remoortel (1), R. Quan (1), Y. Xue (1), I. Appeltans (1), G. Boeckxstaens (1) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing.

Introduction: Macrophages (Mfs) are highly specialized phagocytes that strongly contribute to maintain tissue homeostasis. They not only act as first responders to tissue damage and pathogenic infection, but perform a plethora of tissue-specific functions within a given microenvironment. Intestinal resident macrophages represent a highly diverse population of CX3CR1 expressing cells positioned within the different layers of the intestine. Secluded from the luminal signals, a substantial number of intestinal CX3CR1hi Mfs are found in the muscularis propria in close contact to the myenteric plexus. By applying single-cell RNA sequencing in the gastrointestinal tract of mice, our group recently identified the transcriptome and proteome of the nerve-associated macrophage (NA-Mf) population. Notably, these NA-Mfs exhibited high expression of the tight junction protein F11r (JAM-A) and played a pivotal role in maintaining the health and survival of neurons within the enteric nervous system (ENS). Here we evaluated to what extent this NA-Mf subtype is conserved in other organs and whether they are also closely associated to nerve structures.
Aim: To assess the presence of NA-Mfs in various organs and explore their localisation to nerves beyond the gastrointestinal tract.

Methods: Brain, spinal cord, sciatic nerve, dorsal root ganglia (DRG), heart, lung, liver, pancreas, small intestine, colon, visceral fat, subcutaneous fat, and dermis were isolated from wild type mice. For immunofluorescent analysis, the organs were fixed, embedded in OCT and sectioned after which the tissue sections were stained with F11R, macrophage marker Iba1, neuronal marker Neurofilament F as well as tyrosine hydroxylase and ChAT for confocal imaging (n=3/organ). For flow cytometric analysis (n=8/organ), the different organs were digested to make single cell suspensions which were stained with fluorochrome-labeled antibodies to quantify the F11R+ macrophage population using BD Symphony.
Results: The distribution of F11r+ macrophages among CD64+ macrophages exhibited significant variations across various organs. In more detail, the mean percentages of F11r+/CD64+ macrophages in nervous structures was high: 95.6% in the brain, 94.3% in the spinal cord, 46.8% in the sciatic nerve and 44% in the DRG. Among visceral organs having a various degree of innervation, the percentage of F11R+ macrophages was lower: 43.0% in the liver, 39.3% in the heart, 29.5% in the muscularis of the small intestine and 27.3% of the colon, and 24.8% in the lung. Finally, visceral fat and subcutaneous fat had a low percentage of F11r+ macrophages, with expression levels of 3.9% and 3%, respectively. Next, we quantified F11R+ macrophages by confocal imaging confirming our FACS data. The average percentages of F11+ macrophages are as follows: 95.0% in the spinal cord, 92.7% in the brain, 43.0% in the sciatic nerve, 39.0% in the liver, 37.6% in the pancreas, 31.4% in the small intestine, 30.9% DRG, 30.6% in the heart, 29.0% in the lung, 28.4% in the colon, 11.6% in the dermis, 1.1% in the subcutaneous fat, and 0% in the visceral fat. Finally, we investigated the proximity of F11r+ macrophages to nerve fibers compared to F11r- macrophages using confocal imaging. Compared to F11r-macrophages, F11r+macrophages were significantly closer to neurofilament F+ nerve structures in the lung, skin, pancreas, heart, and liver ($p < 0.0001$). In the small and large intestine, we observed that F11r+macrophages were rather in closer proximity with Hu/CD+ enteric neurons than their F11R- counterparts ($p < 0.0001$, data presented as mean ± SEM).
Conclusions: Using flow cytometry and immunofluorescent stainings we showed that F11R+ NA-Mfs are closely associated with neuronal bodies or nerve fibers in a variety of organs indicating a major role in supporting and protecting both the peripheral and nervous system.

- B16 -

INTERMITTENT FASTING REINFORCES RHYTHMIC ACTIVATION OF INTESTINAL CIRCADIAN CLOCK GENES AND THE GUT TRANSCRIPTOME DURING CHRONODISRUPTION. H. Leng (1), T. Thijs (1), L. Desmet (1), M. Farhadipour (1), I. Depoortere (1) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, gut peptide research.

Introduction: The circadian system enables organisms to optimally adapt their physiological functions and behaviors (activity/rest, feeding/fasting) to the environmental light/dark cycles, ensuring that various processes are carried out at the optimal time of the day. Disturbances of the circadian system as occur during shift work or chronic jetlag, lead to desynchronization of central and peripheral circadian clock genes and are associated with several chronic diseases. During chronodisruption, feeding rhythm becomes an important synchronization signal (known as 'zeitgeber') for the intestinal clock.
Aim: This study aims to investigate whether chronic jetlag affects diurnal fluctuations in the gut transcriptome and whether these disturbances can be prevented using night-time restricted feeding (RF); Additionally, we aim to investigate whether organoids generated from adult jejunal mouse mucosa (enteroids) can serve as a platform to study diurnal rhythmicity of the gut clock.
Methods: Chronic jetlag model: Control mice were housed under a normal light/dark-cycle. Jetlagged mice were shifted between a normal light/dark-cycle (4 days) and a cycle with an 8h time delay (3 days) during 4 weeks. Mice were randomly assigned to three groups: a jetlag group that had ad libitum access to food (JL AL), a jetlag group that was fed a night-time RF diet (JL TRF) and a control group that was fed a night-time RF diet (CTRL TRF). Body weight was monitored. An around-the-clock (4h intervals, 24h) bulk RNA sequencing study was performed on the jejunal mucosa. Enteroid model: Mouse enteroids generated from the jejunal mucosa of Bmal1+/+ and Bmal1-/- mice were synchronized for 1h with 100 nM dexamethasone. Samples for qPCR analysis were taken every 4 hours for 28 hours.
Results: The increase in body weight gain in jetlagged mice was prevented using TRF. The RNA-seq study showed that in the CTRL TRF group, 1985 (18,3%) of intestinal genes were rhythmic, this was reduced to 768 (7,1%) genes in the JL AL group and restored to 2499 (23,1%) genes in the JL TRF group. JL AL induced a shift in the acrophase (time to peak) of 6.7 h ($P<0.001$) of intestinal clock genes (e.g. Bmal1, Rev-erb, Per2) and a phase delay of 5.28 h ($P<0.001$) of intestinal transcripts (176 genes). TRF in jetlagged mice partially prevented these phase shifts to 2.9 h and 1.75 h, respectively compared to the CTRL TRF. Another 322 genes lost their rhythms due to jetlag but were rescued by TRF. Gene Ontology analysis showed that genes, whose rhythms were shifted/lost by JL AL but rescued by TRF, were involved in metabolic processes like nutrient transport, fatty acid β-oxidation, ketogenesis, but also cellular developmental processes such as differentiation and proliferation. The circadian rhythm of intestinal clock genes was maintained in enteroids. The mRNA expression of Bmal1, Rev-erbα and Per2 in the Bmal1+/+ enteroids exhibited diurnal rhythmicity ($Pcosinor < 0.001$) peaking at zeitgeber (ZT) 15h94, ZT 23h92 and ZT 7h69, respectively. In Bmal1-/- enteroids, the rhythmic mRNA

expression of Rev-erbα was lost. Per2 mRNA expression in the Bmal1-/- enteroids was phase advanced by 10h25 and peaked at ZT 21h44 (Pcosinor < 0.05).
Conclusions: TRF during chronic jetlag can resynchronize the rhythms in jejunal clock genes and the gut transcriptome involved in the control of epithelial metabolic homeostasis. Mouse enteroids show rhythms in intestinal clock genes and can serve as a suitable model to study the role of clock genes in vitro.

- B17 -

SINGLE CELL TRANSCRIPTOMICS REVEAL MAST CELL HETEROGENEITY IN THE HUMAN GUT IN HEALTH AND IBS. H. Hussein (1), E. Modave (1), S. Van Remoortel (1), R. Quan (1), M. Delfini (2), G. Boeckxstaens (1) / [1] KUL - University of Leuven, Leuven, Belgium, TARGID, [2] KUL - University of Leuven, Leuven, Belgium, Department of Oncology.

Introduction: Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal disorder characterized by an altered defecation pattern, abdominal pain, and abdominal discomfort, in the absence of an identified organic cause. Aberrant pain signalling, or visceral hypersensitivity (VHS) is a hallmark symptom of IBS and often occurs after eating certain foods. We have recently shown that, in mouse models of VHS, abdominal pain arises due to mast cell degranulation and consequent histamine-dependent sensitization of nociceptive neurons. In those models, a local immune response to the food antigen ovalbumin (OVA) and the production of anti-OVA IgE triggers mast cell activation. However, the phenotype of mast cells in the human gut and in particular in IBS is currently unknown.
Aim: In this study, we aim to determine the phenotype of mast cells in the different layers of the healthy colon and in rectal biopsies of healthy subjects and IBS patients using single cell transcriptomics.
Methods: Five healthy volunteers (HV) who were free of abdominal symptoms, with no history of gastrointestinal disease or previous gastrointestinal surgery were recruited by public advertisement (2M, 3F;18-43 years). Nineteen participants with IBS meeting the ROME III criteria were recruited from the outpatient clinic of the University Hospitals Leuven (3M, 16F; 18-51 years) and further classified into their respective stool subtypes (6 IBS-D, 7 IBS-C and 6 IBS-M). Rectal biopsies (RB) from IBS patients or healthy subjects were taken during proctoscopy. In addition, resection tissue samples from three patients (2M, 1F; 53-68 years) undergoing hemicolectomy for colonic carcinoma were collected and dissected into mucosa, submucosa, and muscularis externa layer. Single cell suspensions of gut samples were obtained by enzymatic digestion following a step of epithelial removal for mucosal layers. Live immune cells (CD45+) were FACS-sorted and were used to prepare single cell RNA-Seq libraries, using the 10X Genomics platform. After de-multiplexing, alignment, and extensive filtering, 280 903 cells from RB and 62 063 cells from colon were integrated at the CD45 level.
Results: To adequately compare mast cell phenotype in health and IBS, mast cell subsets in the healthy colon layers were characterized first. Integration of the dataset of healthy RB and colon layers revealed 4148 mast cells, clustered into five mast cells clusters (MC1-MC5) with distinct transcription factor signatures. MC1 is enriched in the mucosa and is primed for immune cross-talk. MC4 and MC3 both express chymase as well as a neural adhesion molecule and are mainly found in the submucosa and muscularis, respectively. MC5 is only found in RB but not in colon layers. All subsets but one (MC1, MC2, MC4, MC5) were present in RB of HV and IBS patients. Cluster distribution was similar between IBS-D, IBS-C, and HV, but IBS-M only exhibited MC2 and MC5 subsets. 77 genes were differentially expressed between IBS and HV mast cells (log fold change > 0.25, $p < 0.05$). As we previously demonstrated a role for IgE-mediated mast cell activation in IBS, we next investigated changes in population enrichment and gene expression in B cells and plasma cells. Plasma cells and B cells were identified using SDC1 and CD19, respectively. Frequency of plasma cells was increased in IBS-D and IBS-C, while B cells were increased in IBS-M. Interestingly, IGHE expressing plasma cells and B cells were enriched in IBS compared to HV.
Conclusions: We have characterized mast cell populations in the human gut and identified five novel subsets with distinct putative functions and transcription factor expression. Moreover, our results confirm IgE-mediated mast cell activation as a mechanism involved in IBS development in patients.

CASE REPORTS

- C01 -

EARLY PLASMAPHERESIS IN BENIGN RECURRENT INTRAHEPATIC CHOLESTASIS - A CASE REPORT. L. Heyerick (1), A. Dhondt (2), H. Van Vlierberghe (1), X. Verhelst (1), S. Raevens (1), A. Geerts (1) / [1] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology and Hepatology, [2] Ghent University Hospital, Ghent, Belgium, Department of Nephrology.

Case Report: A 43-year-old male patient presented at the hepatology department with complaints of fatigue, insomnia and severe pruritus persisting for four weeks. A diagnosis of a mild covid-19 infection was made three weeks earlier, which did not require specific treatment. The patient's pruritus symptoms were unresponsive to antihistaminic therapy. Clinical examination revealed jaundice without additional abnormalities. Laboratory results showed markedly elevated levels of total (16.7 mg/dL) and direct (14.3 mg/dL) bilirubin, increased alkaline phosphatase (ALP, 2.9x ULN) and mildly elevated transaminases (<1.5x ULN). Gamma-glutamyltransferase values were normal. A previous diagnosis of benign recurrent intrahepatic cholestasis (BRIC) type 2 had been established at the age of 22, after he experienced repetitive similar flares of cholestasis that lasted for several months and eventually resolved spontaneously. In between two flares, he did not have any symptoms. Genotyping confirmed compound heterozygosity (Glu297Gly; Ile1227Phe) in the ABCB11 gene. Since diagnosis, over the course of two decades, he had already experienced five independent flares of BRIC that lasted on average for four months. Consequently, a new flare of BRIC was diagnosed based on the current clinical presentation and past history. Treatment with cholestyramine and rifampicin was ineffective. Accordingly, nasobiliary drainage was attempted but this was terminated early due to relapsing obstruction and ineffectiveness. Intermittent plasmapheresis was then started, 1.5 months after flare onset, and this rapidly alleviated pruritus symptoms, with complete normalization of lab results achieved after 11 plasmapheresis sessions over the course of three months. 1.5 years later, at the age of 45, the patient experienced another mild covid-19 infection which, after one month, was followed by a new prototypical episode of BRIC, with severe pruritus and laboratory results showing beginning signs of cholestasis with mildly elevated total (1.5 mg/dL) and direct (0.8 mg/dL) bilirubin and increased ALP (2.4x ULN). Early initiation of intermittent plasmapheresis, 10 days after flare onset, led to complete symptom resolution after two sessions over four days, and normalized biochemical markers of cholestasis after two weeks. BRIC is part of a group of rare, inherited cholestatic liver diseases and is characterized by relapsing episodes of cholestasis with severe pruritus and jaundice. Episodes last from weeks to months and can be triggered, most frequently by a recent infection. Between two episodes, patients are symptom-free and have normal liver biochemistry values. The overall prognosis is favorable and patients typically do not develop liver fibrosis or cirrhosis. BRIC is subdivided in two subtypes, based on the affected hepatocanalicular transporter gene (ATP8B1 in BRIC type 1 and ABCB11 in BRIC type 2). Antipruritic pharmacological therapies, including cholestyramine, rifampicin, naltrexone and sertraline, show variable results in patients with BRIC. Nasobiliary drainage interrupts the enterohepatic circulation and is an effective but invasive procedure for relieving pruritus. Furthermore, its use is constrained by technical limitations, such as drain obstruction. Plasmapheresis or artificial extracorporeal liver support (Prometheus®) may be considered to eliminate circulating pruritogens when other therapies fail. Plasmapheresis is a widely available and affordable technique. In contrast, Prometheus® is an expensive and labour-intensive therapeutic intervention that can only be employed in a limited number of centres. This case report highlights the efficacy of early plasmapheresis in rapidly improving pruritus symptoms and in prematurely terminating cholestasis episodes. Early consideration of plasmapheresis is warranted upon the diagnosis of a new BRIC flare.

- C02 -

NEOADJUVANT APPROACH OF AN UNRESECTABLE RECTAL GIST. C. Brackenier (1), K. Van der Speeten (2), J. Vannoote (3), C. Severi (3) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [2] Ziekenhuis Oost Limbug (ZOL), Genk, Belgium, Abdominal Surgery, [3] Ziekenhuis Oost Limbug (ZOL), Genk, Belgium, Gastroenterology and Hepatology.

Case Report: A 57-year-old female was referred to the department of Gastro-enterology because of a pelvic mass. Her medical history consisted of lumbar discus hernia and hypothyroidism. Her complaints were a fluctuating stool pattern and a vague lower abdominal pain. She intentionally lost 3 kilogram in weight due to dietary measurements. Laboratory tests showed normal inflammatory parameters, functional iron deficiency (transferrin saturation 12%) and elevated lactate dehydrogenase (LDH) (365 U/L). An immune faecal occult blood test was normal. Abdominal ultrasound revealed a voluminous necrotic mass. Magnetic resonance imaging of the pelvis confirmed (1) a tumoral lesion of 10x10x11 cm with compression of rectum, vagina and cervix but without clear invasion in the surrounding structures, (2) a preserved internal anal sphincter, (3) no adenopathies and (4) a small diffusion restrictive lesion in the ilium. Positron emission tomography and computed tomography (PET-CT) showed high fluorodeoxyglucose(FDG)-avidity of the pelvic tumoral mass and could not withhold other lesions, especially not at the ilium. Endoscopic evaluation withheld normal rectal mucosa but severe narrowing of the rectal lumen due to suspected external compression. A biopsy of this bulging revealed

spindle-shaped CD34+ and CD117+-cells, which findings correspond to a cKIT-positive gastrointestinal stromal tumor (GIST). Following a multidisciplinary team meeting the tumor was considered unresectable due to proximity to different surrounding organs. Perhaps a pelvic exentration was possible after downstaging. Systemic therapy with imatinib 400 mg daily was started. After one week the patient reported an immediate relief of her complaints. A re-evaluation with PET-CT after 4 weeks showed a spectacular shrinkage of the tumor and decrease of avidity of the lesion. Therefore, imatinib was continued for 8 more weeks. Following this, tumor regression was consistent with a further decrease in volume of the lesion towards 6x6x8 cm, a decrease in compression of surrounding tissues and a total loss of FDG-avidity on PET-CT. Furthermore, LDH was normalized. The tumor was now considered resectable and an abdominoperitoneal rectum amputation (APRA) with ovariectomy and hysterectomy was performed with clear surgical margins. There was no need for resection of the bladder. Histology of the resection specimen confirmed a cKIT-positive GIST with 4 mitoses per 5 mm², tumor-free resection margins, ypT3N0. Currently, the patient receives adjuvant imatinib 400mg daily for a period of 3 years. Until now, there have been no problems in the follow-up. Discussion: In this case imatinib showed a spectacular effect in a neoadjuvant setting in rectal GIST. GIST is the most common mesenchymal neoplasm of the gastrointestinal tract. Rectal GIST is a rare condition and accounts only for 5% of all GISTs. This case is remarkable given the impressive and fast tumor response. Clinical symptoms were resolved after only 1 week. A consistent reduction of tumor size and involvement with surrounding organs was achieved and furthermore FDG-avidity had completely disappeared. Imatinib successfully turned the unresectable GIST into a resectable tumor in a short period of time and made a curative intent possible. Furthermore, surgery was less invasive and resulted in a quick recovery. Conclusion: Imatinib has the potential to have a robust and fast tumor response in cKIT-positive rectal GISTs. Therefore, it can turn unresectable tumors towards curative settings.

- C03 -

RECTAL TUMEFACTION AS A PRESENTATION OF SECONDARY SYPHILIS. V. Chua (1), M. de Ryckel (2), R. Ntounda (3), L. Sabor (4), D. Schoonbroodt (2) / [1] CHU UCL Namur site Sainte Elisabeth, Brussels, Belgium, Internal medicine, [2] CHU UCL Namur site Sainte Elisabeth, Brussels, Belgium, Gastroenterolgy, [3] CHR, Namur, Belgium, Gastroenterolgy, [4] CHR, Namur, Belgium, Medical Biology.

Introduction: Syphilis is a sexually-transmitted infection caused by the spirochete Treponema Palidum, which can rarely mimic a rectal tumor and therefore is often called “the great imitator”. Syphilis has been reported as a re-emerging STIs by the WHO (1). In 2018, men accounted for 86% of all patients with syphilis (2). In Belgium, men who have sex with men (MSM) are the most affected population explained by high rates of unprotected sex (3). Syphilis develops in three stages separated by asymptomatic or latent periods, only primary and secondary stages are contagious. We insist on the importance of diagnosing it quickly as it can lead to multiple neurologic and cardiovascular complications, and eventually be a lethal disease if untreated. Syphilis has a huge gastroenterologic interest as it can mimic several common diseases such as Crohn diseases (4) or rectal mass (5), causing typical digestive symptoms that could bring the patient into consulting a gastroenterologist. Rectal syphilis can be difficult to diagnose, especially when encountered by endoscopy it can easily be misdiagnosed as a malignant rectal tumor. As healthcare professionals it may not be easy to speak about STIs with patients, but it is an essential discussion to have when suspecting a possible sexually transmitted rectal disease. In this case we’d like to reassess the importance of asking the right questions when facing a rectal lesion, as we report a rare case of secondary syphilis presenting as a rectal tumefaction.
Case Report: We report a case of a 45-year-old patient presenting himself at the emergency department for constipation and rectal bleeding. The patient has no particular medical history and isn’t on any medication. He does smoke about 15 cigarettes a day and drinks 1 glass of whisky per day. He lives with his wife with whom he has been married for 25 years. The patient has not had a bowel for 3 days at the time he arrives in the emergency department. The biology showed a minor inflammatory syndrome (CRP 22,7mg/L), cholestasis (GGT 1568U/L, PAL 652 U/L), nonspecific leukocytosis (10100 WBC/L). A rectal examination showed a clear induration which motivates a rectoscopy the same day. The rectoscopy is performed and shows a large, indurated and ulcerated lesion of the lower rectum. A malignant rectal lesion is therefore suspected. A thorax and abdominal CT-scanner is done and showed a voluminous rectal tumor lesion with diffuse infiltration of the mesorectum and multiple adenomegaly in the mesorectum, intra-aortic-caval area and along the left iliac axis. There were also several pulmonary micronodules at both bases, the largest measuring 7 mm. From there, an echo-endoscopy is performed to collect biopsies. The rectal mass is described as a curvature beginning after the anal canal, extending to the middle third and one-third of the circumference anteriorly, with an extrinsic appearance and a poorly expansible. No other colic lesions were described. First biopsies came back negative. A second endoscopy is performed in another center showing granulomatous lesions. When we discussed the situation with the patient once more, he finally told us that he was having MenWithMen receptive sex in a swingers club, attending alone without his wife every weekend. We then asked for syphilis serology that came back with a positive TPHA title of 1/10240 and a RPR at 1/32, titles that can apply for a secondary form of treponematosis syphilis. The syphilis serology was analyzed with a Liaison Treponema Screen test using immunoanalysis on a Liaison Analyzer. TPHA and RPR were analyzed using a Spinreact hemagglutination kit. HIV serology came back negative. There was no history of syphilitic chancre in this case. The patient was treated by intramuscular benzathine penicillin at the dose of 1,2 millions units per buttock the first day

then again one week later. The patient's biological tests became normal weeks later. The rectal bleeding stopped quickly after treatment.
Conclusion: Rectal presentation of syphilitic infection can be difficult to diagnose, and sometimes needs multiple biopsies to be confirmed, which can lead to a late diagnosis. The key to an early diagnosis may rely on a proper anamnesis, in taking the right amount of time and being able to communicate and create a safe space for patients to express themselves without feeling judged. Syphilis is a re-emerging disease worldwide (1) that we should bring more focus on regarding the gastroenterologic approach. The gastroenterologist can indeed encounter several cases and therefore prevent the severe complications of the disease by a quick diagnosis and therefore a more rapid treatment.
Discussion: Syphilis can mimic a lot of different diseases by the wide kind of symptoms that can occur after the presence of treponema pallidum in different areas and organs of the body. Although it is not a very often encountered disease in gastroenterology, its prevalence in developed countries is rising. About this case, the main difficulty was to get the right information from the patient that could have led us directly to the diagnosis instead of waiting for the anatomopathological investigations. Therefore it should be discussed to include syphilis serologies in the standard differential diagnosis of rectal mass discovered in men with no other risk factors of colorectal cancer.
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- C04 -

DIARRHEA IS NOT A VIP GUEST. L. Mans (1), M. Pezzullo (2), P. Demetter (3), I. Tancredi (4), P. Loi (5), A.-M. Bucalau (1), M. Arvanitakis (6), J.-L. Van Laethem (1), A. Hadefi (6) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology and Digestive Oncology, [2] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Radiology, [3] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Pathology, [4] CHU de Charleroi, Hôpital Marie Curie, Charleroi, Belgium, Radiology, [5] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Digestive Surgery, [6] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology.

Case Report: A 72-year-old man who underwent corporal-caudal pancreatectomy in June 2018 for a well-differentiated grade 1 neuroendocrine tumor (Ki67: 2% upon diagnosis) who has been followed up in our institution since June 2022 for liver recurrence. Further work-up using 18F-fluorodeoxyglucose PET/CT and 68Ga-DOTATOC PET/CT confirmed exclusive hepatic recurrence. A liver biopsy revealed a grade 2 neuroendocrine tumor with Ki67 at 15.3%. Treatment with somatostatin analogue such as Somatuline autogel at a dosage of 120mg every 28 days was initiated with disease control until April 2023, where a thoraco-abdominal CT scan showed progression of liver lesions. At the same time, the patient was admitted to hospital for altered general condition, watery diarrhea, hypotension and weight loss. Blood test revealed an acute renal failure with urea at 115 mg/dl and creatinine at 1.88 mg/dl, hypokalemia at 2.2 mmol/l and metabolic acidosis. The patient required intravenous and oral potassium supplementation up to 180 mEq per day to achieve a potassium level of 3.5 mmol/l, as well as daily sodium bicarbonate supplementation. Daily parenteral nutritional support was also introduced. Stool cultures revealed a Blastocystis hominis infection treated with Flagyl without any clinical improvement. Given the persistence of diarrhea, the aforementioned investigation was repeated but did not reveal further pathogen. A colonoscopy was performed with random ileal and colon biopsies which did not yield any histological diagnosis. Empirical treatment with colestyramine showed no efficacy. A combination of treatment with loperamide, pancreatic enzyme supplementation and codein syrup resulted in a mild reduction in diarrhea. Based on the severe presentation of hypokalemia and metabolic acidosis, a vipoma was suspected and vasoactive intestinal peptide (VIP) level was measured at 918 ng/l (N< 101 ng/l). The second test confirmed high level value of VIP, which was of 1398 ng/l, thereby the diagnosis of VIPoma was made. A work-up using 18F-fluorodeoxyglucose PET/CT and 68Ga-DOTATOC PET/CT was done, ascertaining absence of extrahepatic lesions. Therefore, we decided, in multidisciplinary board for neuroendocrine tumors, to perform hepatic arterial. The patient underwent bland embolization of the right liver, followed by left liver embolization two weeks later. Continuous infusion of somatostatin analogue was started along with hepatic embolization during his admission, and afterwards relayed subcutaneously. This treatment was associated with a complete resolution of the diarrhea, hypokalemia and metabolic acidosis allowing treatment discontinuation a couple weeks later. Patient gained weight and consequently parenteral nutrition was weaned off. A thoraco-abdominal CT scan, performed 2 months after embolization, showed a partial response.
In conclusion, VIPoma are rare functioning neuroendocrine tumors with high plasma levels of VIP secretion. The first treatment consists in correction of fluid and electrolytes imbalance. Somatostatin analogue reduces diarrhea, allowing

to mitigate dehydration and electrolyte disorders. Surgery should be performed in cases of locoregional disease. For liver-dominant disease, targeted treatment is recommended, such as bland embolization, radiofrequency ablation, and radioembolization. Other treatments such as Everolimus, Sunitinib, peptide receptor radionuclide therapy (PRRT) or chemotherapy are alternatives for metastatic or unresectable disease.

- C05 -

A CASE OF RECURRING CHOLANGITIS DUE TO AN HILAR OCCLUDING UNCOVERED SELF-EXPANDABLE METAL STENT: TRIPLE METAL STENTING OF THE HEPATIC BILE DUCTS USING A RENDEZ-VOUS APPROACH AND HEPATICOGASTROSTOMY. M. Staessens (1), T. Jardinet (2), W. Kwanten (1), T. Steinhauser (1), H. De Schepper (1), A. Jauregui Amezaga (1), M. Somers (1), S. Bouhadan (1), K. Krishnadath (1), S. Francque (1), E. Macken (1) / [1] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology and hepatology, [2] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Radiology.

Case Report: A 76-year-old male was admitted to the Antwerp University Hospital due to feeling unwell since 3 weeks, with the development of shivering on the day of presentation. He had no fever, no respiratory, cardiac, gastrointestinal or urinary complaints on system history. He had a well-known but stable cardiomyopathy and third degree AV nodal block for which he received an implantable cardioverter-defibrillator (ICD). Moreover, his medical record revealed a hilar cholangiocarcinoma in 2015 (not proven on biopsy) for which he had received chemotherapy for 2 years, after which the treatment was halted due to supposed tumoral regression. Due to biliary obstruction he received an uncovered self-expanding metal stent (SEMS) in the right ventral hepatic duct in a peripheral hospital in 2015. Finally, he had a cavernous malformation due to a portal vein thrombosis with secondary atrophy of the left liver lobe. On clinical examination, he appeared well and there were no apparent abnormalities. The vital signs were within the normal range. Initial lab results revealed a mildly elevated total bilirubin of 1,5 mg/dL, with a conjugated bilirubin of 1,2 mg/dL, ALT 24 U/L, AST 38 U/L and GGT 69 U/L. Liver synthetic function tests were normal. His inflammatory parameters were elevated, with a C-reactive protein of 113 mg/L and elevated white cell count of 11,3 x 10^9/L. Blood cultures revealed a sepsis with Citrobacter freundii and Klebsiella aerogenes, for which targeted antibiotic therapy was commenced. On first imaging with transabdominal ultrasound and an abdominal CT scan, dilated intrahepatic bile ducts were seen. Other foci of infection were ruled out by a PET-CT scan. An ERCP was subsequently performed due to suspicion of a stent occlusion, however with balloon extraction no apparent stenosis nor occluding debris were noted. We were unable to selectively cannulate the left hepatic duct and the right posterior hepatic duct due to hilar ingrowth of the uncovered SEMS, which was placed in the right ventral hepatic duct. A percutaneous approach was performed, leaving two external drainage catheters via the posterior hepatic duct as it was impossible to pass a guidewire through the SEMS to achieve internal-external bile duct drainage. The inflammatory lab subsided and the patient went well. However, the patient complained of a reduced quality of life due to the external drainage catheters and proclaimed the wish to internalize the bile duct drainage. After discussing the potential risks and benefits of further invasive treatments with the patient and at a multidisciplinary team meeting, we performed a percutaneous cholangioscopy via the right posterior hepatic duct with the intention to disintegrate the SEMS using argon plasma coagulation (APC). However, we were unable to approach the SEMS due to limited intraductal mobility of the cholangioscope. Thereafter, we attempted a rendez-vous procedure in which the radiologist was able to pass a guidewire via the right posterior hepatic duct through the maze of the SEMS, into the duodenum. Simultaneously, an ERCP was performed in which the SEMS was cannulated deep into the right ventral duct. Two uncovered SEMS of 100 x 80 mm (M-stent, 6 Fr delivery system, Taewoong) were deployed at the same time: one in a percutaneous anterior fashion (proximal end in the right posterior duct, distal end in the duodenum) and one in a retrograde fashion through the ERCP working channel (proximal end in the right ventral duct, distal end in the duodenum). To ensure drainage of the entire biliary tree, an uneventful endoscopic hepaticogastrostomy (Giobor stent 100 x 80 mm, Taewoong) was performed the week thereafter. The patient recovered and was discharged about two weeks after the final procedure, free of external drainage catheters. There was no recurrence of a cholangitis as of yet. We describe a case of recurrent cholangitis due to hilar obstruction of an indwelling uncovered SEMS, which has been successfully treated by using a percutaneous rendez-vous procedure and hepaticogastrostomy resulting in bile duct drainage of the three major hepatic ducts (right dorsal, right ventral and left hepatic duct).

- C06 -

COMBINATION THERAPY BASED ON SPYGLASS-GUIDED ELECTROHYDRAULIC LITHOTRIPSY THROUGH A CHOLECYSTODUODENOSTOMY BY LUMEN-APPOSING METAL STENT (SLAMS) FOR MIRIZZI SYNDROME. V. VandenDriessche (1), P. Yengue (1), J. Collin (1), M. Lefebvre (1) / [1] Centre Hospitalier Wallonie Picarde (CHWAPI), Tournai, Belgium, Gastro-Entérologie.

Case Report: Mirizzi syndrome is a rare complication of chronic gallstone disease characterised by the compression of the common bile duct due to an impacted lithiasis in the infundibulum of the gallbladder or cystic duct. This compression leads to inflammation and cholestasis, which can result in complications such as fistulae, acute pancreatitis, cholangitis or

septic shock if left untreated. Laparoscopic cholecystectomy has been used for the treatment of Mirizzi syndrome since 1987. However, open cholecystectomy remains the standard of care for Mirizzi syndrome due to an elevated risk of bile duct injury and a high conversion rate when the laparoscopic approach is used. Nevertheless, surgery may not always be feasible, especially in elderly patients or those with multiple comorbidities. This is especially pertinent in a globally ageing population, therefore increasing the need for minimally invasive therapeutic strategies. Prior studies have highlighted the increasing role of lumen-apposing metal stents (LAMS) in managing gallbladder drainage when endoscopic retrograde cholangio-pancreatography (ERCP) is not feasible. Additionally, the clinical efficacy of SpyGlass-guided lithotripsy has been demonstrated for the treatment of large common bile duct and cystic duct stones. To our knowledge, there are no prior literature reports combining these two techniques for the management of biliary obstruction. The aim of this study is to combine SGEHL and LAMS, abbreviated SLAMS, as a less invasive treatment option for inoperable patients with Mirizzi syndrome. In this case study, we present an 85-year-old patient who was not eligible for surgery due to her advanced age and frailty. She was admitted through the emergency department and presented with septic shock of biliary aetiology. Broad- spectrum antibiotics and IV hydration were promptly administered after onset of hypotension, jaundice and fever. The initial blood workup revealed elevated bilirubin levels, raised liver enzymes, increased gamma-glutamyl transferase (GGT) and alkaline phosphatase (ALP) levels. Additionally, there was an upsurge in inflammatory markers such as C-reactive protein (CRP), along with raised leukocyte and neutrophil counts. Our initial attempt to improve the patient's clinical condition through ERCP with sphincterotomy, lithiasis extraction using a balloon catheter and placement of a plastic biliary stent in the common bile duct was only partially successful. Furthermore, a bile fluid culture sampled during the ERCP procedure, returned positive for Escherichia coli and Enterococcus faecalis. As a consequence of the ERCP, jaundice decreased; however, abdominal pain in the right hypochondriac region and sepsis persisted. The lack of complete clinical resolution was attributed to an additional lithiasis of approximately 20 mm in diameter lodged in the cystic infundibulum, a characteristic feature of type I Mirizzi syndrome. As a result, we opted for an alternative approach, an endoscopic ultrasound-guided cholecystoduodenostomy by LAMS with a diameter of 15mm to initiate gallbladder drainage. We then utilised this bulbo-cholecystic LAMS the following week to fragment the isthmic bile stone by performing SGEHL passing through the aforementioned LAMS. We then extracted the remaining biliary debris by endoscopic forceps and loop. Thanks to successful fragmentation of the isthmic lithiasis, no recurrence of cholestasis was observed after the removal of the plastic transpapillary stent. Most blood analyses returned to normal within seven days post- SLAMS, including bilirubin levels and leukocyte counts. We additionally noted a substantial reduction in alanine aminotransferase (ALT), aspartate aminotransferase (AST) and CRP levels post-SLAMS. GGT levels also showed improvement, but a minor increase in ALP was observed. We hereby establish proof of concept demonstrating the successful treatment of type I Mirizzi syndrome using a novel combination approach called SLAMS, which combines SGEHL and a cholecystoduodenostomy by LAMS. While previous case reports have shown success in treating Mirizzi syndrome by combining SGEHL and ERCP, to our knowledge, our study is the first to combine SGEHL and LAMS for this condition.

V. VandenDriessche, P. Yengue, J. Collin and M. Lefebvre. Combination therapy based on spyglass-guided electrohydraulic lithotripsy through a cholecystoduodenostomy by lumen-apposing metal stent (SLAMS) for Mirizzi syndrome. Accepted for publication in Acta Gastroenterologica Belgica. Sept 2024. Vol. 87 (3).

- C07 -

GASTROENTEROLOGY STRIKES THE BRAIN. P. Vanuxem (1), D. Persyn (1), G. Lambrecht (1), G. Deboever (1), M. Cool (1) / [1] AZ Damiaan, Oostende, Belgium, Gastroenterology.

Case Report: A 67-year-old man presented to the emergency department with motor aphasia and right hemianopsia, suggesting acute stroke. CT-imaging of brain and vessels showed no cause and an MRI of the brain was negative despite persistence of symptoms. Biochemistry did however show profound hypomagnesemia (0.117 mmol/L; reference 0.66-0.99 mmol/L) and intravenous magnesium substitution caused rapid symptom recovery. Stroke mimic due to hypomagnesemia was the diagnosis as we found no other cause. Retrospectively, patient was known with significantly gastroesophageal reflux disease (GERD) for which he had been taking a proton pump inhibitor (PPI) for many years. The PPI was stopped and the hypomagnesemia did not recur so far. That PPIs can cause hypomagnesemia is well known(1). However, the exact mechanism is not yet fully understood. The current hypothesis is that it is caused by impaired intestinal absorption of magnesium, due to different mechanisms induced by PPIs (affecting paracellular transport of magnesium in small intestine and colon, change in gut microbiome…)(2). Both dose and duration of treatment increase risk (3,4). Common symptoms of hypomagnesemia are neuromuscular and cardiovascular (5). Occasional in severe hypomagnesemia, a stroke-like picture may occur(6). There is no evidence based treatment at this point for this adverse effect of PPIs. Cases have shown that substitution of magnesium only is not sufficient, as continuing PPIs gives recurrence of hypomagnesemia. Withdrawal of the PPI seems to be the only effective treatment on long term (2). This case illustrates a rare expression of a common side effect of a widely used drug. We think that this should further draw our attention to screening for hypomagnesemia in PPI-users. Furthermore, it is important to only give PPIs when there is a hard indication, in the right dose and for an appropriate duration. Also further research is needed to explore the underlying mechanism of PPI-induced hypomagnesemia and maybe to look for safer treatment options in people with GERD.

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- C08 -

IGG4-GASTRODUODENITIS IN A CASE OF ISOLATED UPPER GI CROHN'S DISEASE. V. Desmedt (1), J. Geldof (2), A. Hoorens (3), T. Lobaton (4) / [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] Ghent University Hospital, Ghent, Belgium, Department of Pathology, [4] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology and Hepatology and Department of Internal Medicine and Pediatrics.

Case Report: We report the case of a 20-year-old man, with previously unremarkable medical history, presenting with epigastric pain and 10 kg weight loss over the past six months. He also reported early satiety, nausea without vomiting and looser stools since a couple of months. The patient was an active smoker and had regular alcohol consumption. He did not recently use non-steroidal anti-inflammatory drugs (NSAID) nor any maintenance medical treatment. Vital parameters were normal and physical examination showed no abdominal abnormalities. Initial laboratory testing showed a mild thrombocytosis (394000x10E3/µL) and a mild elevation of aspartate aminotransferase (84 U/L; normal < 37 U/L) and alanine aminotransferase (92 U/L; normal < 40 U/L) with no alterations in other liver function tests. IgE titer was remarkably elevated (758 kU/L (0-100 kU/L). Fecal calprotectin was slightly elevated (130,9 mg/kg, reference < 50 mg/kg). In another hospital, an esophagogastroduodenoscopy (EGD) revealed a bumpy and erosive appearance of the gastric mucosa and bulboduodenal ulcerations with stenosing effect causing gastric outlet subobstruction. The biopsies showed chronic active, Helicobacter pylori (HP) negative gastritis and bulbitis. There were no signs of malignancy and no granulomas were observed. Pantoprazole 40mg BID was started. Control EGD few months later at our center, showed similar macroscopic findings despite proton pump inhibitor (PPI) treatment. Repeated extensive biopsy sampling confirmed persistent acute bulbitis and HP-negative, chronic active gastritis. Periodic acid-Schiff stain gave no arguments for Whipple's disease. An abdominal computed tomography, ileocolonoscopy with ileal and colonic biopsies and a magnetic resonance enterography did not show other locations of intestinal inflammation. Screening for Zollinger Ellison syndrome showed a mildly elevated serum gastrin level (339 ng/L) on PPI and 68Ga-DOTA-1-NaI3-octreotide (DOTANOC) Positron Emission Tomography (PET)-CT showed no elevated somatostatin receptor expression. MR enterography and additional endoscopic ultrasound (EUS) of the pancreas showed no arguments for a primary neuro-endocrine tumor. There were no serological or histopathological arguments for auto-immune gastritis. Tuberculosis and sarcoidosis were excluded. After this profound work-up the patient was referred to our inflammatory bowel disease (IBD)-unit and a repeat EGD with biopsies showed erosions in the stomach with the known stenosis of the pylorus and a large ulcer at the transition from the pylorus to the bulbus and multiple punched-out ulcerations In the duodenum. The gastric biopsies showed a few small non-caseating granulomas, suggestive of Crohn's disease (CD), since other causes of granulomatous gastritis, i.e. sarcoidosis, malignancy, infectious diseases like tuberculosis or Whipple's disease, had already been thoroughly ruled out. In addition, because of persistent ulcerative gastritis with stenosis, despite high doses of PPI, IgG4 staining was performed to rule out IgG4-related disease, and the number of IgG4-positive plasmocytes was found to be significantly elevated on both gastric and duodenal biopsies. In the corpus of the stomach, the number of IgG4-positive plasma cells was highest with more than 50 IgG4-positive plasma cells per high power field (HPF) and an IgG4/IgG ratio above 40%. An elevated immunoglobulin G4 (IgG4) was seen in serum (194 mg/dl, reference values 8-140 mg/dl). Based on these clinical, serological, radiological, and histopathological findings, the presumptive diagnosis of an overlap of gastric CD and IgG4 gastroduodenitis was made, as granulomas are unlikely in IgG4-related disease. Treatment with anti-TNF (Infliximab) in combination with azathioprine, started after the initiation of a methylprednisolone 32 mg/day tapering course, showed a good response, clinically and endoscopically with resolution of the subobstruction. However, active chronic inflammation with increased IgG4-positive plasma cells (>100 IgG4-positive plasma cells/HPF) remained present in the duodenal biopsies. Gastric biopsies showed inactive chronic gastritis with up to 14 IgG4-positive plasma cells/HPF.

Discussion: In this case, an overlap between IgG4-gastroduodenitis and upper GI Crohn's disease is suspected. It shows the importance of a thorough work-up in patients with refractory, ulcerative gastroduodenal inflammation, in which IgG4-related disease needs to be considered in the differential diagnosis (1) To date, conflicting data on IgG4-levels in IBD are published and it is unclear whether high mucosal IgG4-levels in IBD patients are a separate disease entity or a marker of aggressive course (2-3). (1) Sawada H, Czech T, Silangcruz K, Kozai L, Obeidat A, Wien EA, et al. Clinicopathological

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- C09 -

PSEUDO-SIGNET RING CELLS: A BLESSING IN DISGUISE. M. Vanhooren (1), A. Billiet (1), T. Hendrickx (1), J. Vancanneyt (1), F. Van Herpe (1), H. Topal (2), G. De Hertogh (3), X. Sagaert (3), J. Dekervel (1), G. Rasschaert (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Abdominal Surgery, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Pathology.

Signet ring cells (SRC) are characterized by a cytoplasmic vacuole displacing the nucleus to the periphery of the cell in a crescent-shape. When the nuclei of the cells are hyperchromatic, pleomorphic and manifest mitoses, when the vacuole contains mucus and when the cells are eventually infiltrating the lamina propria, this represents the histologic hallmarks of signet ring cell adenocarcinoma (SRCA). SRCA can arise from a number of tissues, however they are most frequently seen in gastric cancer where it accounts for approximately 30% of cases also annotated as diffuse-type gastric cancer. This histologic subtype is appreciated to have a worse prognosis compared to intestinal-type gastric cancer. However there is an histological entity morphologically mimicking SRCA but without infiltrative characteristics: pseudo-signet ring cells (pSRC).

Case reports: We report two striking cases from our clinic with far-reaching consequences. A 61-year-old male was seen in our outpatient clinic for a second opinion. Routine random gastric biopsies taken during an esophagogastroduodenoscopy (EGD) for follow up of a Barrett's esophagus, in an otherwise healthy patient without any complaints, showed SRC at the fundus, suggesting the diagnosis of a diffuse-type gastric cancer. Repeat EGD was negative for any visible lesions, an extensive mapping was pursued. This time SRC were found in random antrum biopsies, the other anatomical gastric locations were all negative. Endosonography evaluation was negative. Staging for distant metastases by means of an FDG-PET-CT was also negative. Peri-operative systemic treatment with FLOT was proposed. After one administration the patient was seen at our emergency department with suggestive complaints of coronary spams. Meanwhile expert pathology revision at two other institutes than the first one, concluded independently from each other for a clear case of pSRC. In this context, and after thorough discussion with the patient it was decided to interrupt the oncology treatment. Another control high definition EGD in expert hands, again with extensive mapping, at a relative distance from the previous EGD, was planned. This ultimate EGD and its pathology were negative: not a single SRC neither SRCA nor pSRC was retrieved. Today we are one year further, the patient is doing perfectly fine. A 59-year-old male with hematemesis was diagnosed with an intestinal-type gastric cancer at the antrum, clinically staged cT2N1. After four cycles of systemic treatment by means of FLOT it was decided to perform a distal gastrectomy with D2 lymphadenectomy. The pathology report disclosed a pathological complete response (pT0N0) in the context of extensive intestinal metaplasia. Four more cycles of FLOT were administered to complete the perioperative chemotherapy lege artis. Six months later a new EGD was done for an aspecific sign of CT-graphic thickening of the stomach wall. Endoscopically sole erythematous gastropathy was observed. However pathology reported on SRC, but advised upon repeat EGD because of the possibility of pSRC in the context of conserved E-cadherin expression, a low Ki67 proliferation index and the absence of abberant p53 expression. Staging FGD-PET-CT was negative. Repeat EGD one month later was negative on pathology. Although these assuring clinical findings, and despite a totally different physiopathological cascade for diffuse-type versus intestinal-type gastric cancer, it was decided after discussion with the patient to perform a completion gastrectomy. Pathology was negative for SRCA and pSRC. While pSRC are mimickers SRCA, they are rare and thus literature is rather scarce. pSRC seem to potentially arise in the context of injury and stress (e.g. ischemia, ulceration, reactive gastropathy). The lack of infiltrative features should trigger the possibility of pSRC. Blinded pathology revision and eventual new biopsies at a relative distance in time can be advised in case of doubt. These two cases clearly illustrate the far-reaching consequences whenever pSRC are wrongly perceived as SRCA. Awareness among pathologists, gastroenterologists, surgeons and oncologists should be encouraged.

- C10 -

IT'S NOT ALWAYS IBD. H. Cherkaoui (1), N. Lahmidani (2), A. Mekkaoui (2), M. El Yousfi (2), D. Benajah (2), S. Ibrahimi (2), M. Abkari (2), H. Abid (2) / [1] Hôpital Civil Marie Curie, Lodelinsart, Belgium, Gastro-Entérologie, [2] University Hospital Hassan II, Fez, Morocco, Gastroenterology.

Case Report: We report the case of a 26-year-old female patient from a first-degree consanguineous marriage with a history of repeated respiratory infection, whose brother died in childhood from a severe respiratory disease. She consulted

in October 2019 for bloody diarrhea that started two weeks earlier. Screening for common GI infections, including C. difficile, was negative. The endoscopy showed an erythematous ulceratibe continuous rectosigmoiditis (Image 1), and the rest of the colon was regular. Pathology showed basal plasmacytosis and crypt architectural distortion. EGD was normal. CT scan showed a sigmoid thickening and no signs of inflammation in the small bowel. She was treated as ulcerative colitis and put on mesalazine and corticosteroid therapy with an excellent initial clinical response, then initiation of azathioprine at a dose of 2 mg/ Kg/ day. The patient was admitted in January 2021 for apyretic cholestatic jaundice and febrile right hypochondrium pain. At admission, she had bilateral thoracic condensation syndrome, dacryocystitis, and erosive facial lesions. Biology showed elevated leucocytes, lymphopenia, and hyperbilirubinemia. A complete viral check-up in search for viral hepatitis, HIV, herpes, EBV was negative. Protein electrophoresis showed hypogammaglobulinemia at 5.6 g/L with decreased IgG levels; the IgG4 subpopulation was normal. The lymphocyte subpopulation assay was average, but HLA DR expression was negative. The rest of the immune check-up was regular: the dosage of complement factor, explosion of neutrophils, anti-pneumococcal and tetanus antibodies. In addition, autoimmune workup showed positive anti-nuclear antibodies. Abdominal CT scan showed a normal-sized, homogeneous liver with moderate dilatation of the main bile duct measuring 10 mm without visible lithiasis and inflammatory stricture of the lower bile duct. The thoracic scan showed a bilateral interstitial syndrome, and urine analysis showed an acinetobaumani sensitive to Imipenem. The patient was put on steroids and Imipenem for ten days with an improvement of jaundice and the disappearance of the bile duct stenosis in the MRI, and thus ERCP was not necessary. A liver biopsy showed peri-portal lymphoplasmacytic infiltrate without granuloma (A1F0). There was no evidence of autoimmune disease or small duct sclerosing cholangitis. The diagnosis was an HLA-DR deficiency based on clinical criteria due to respiratory digestive cutaneous and infectious involvement. The biological criteria were hypogammaglobulinemia, lymphopenia, and HLA-DR deficiency. The genetic study by PCR-sequencing showed a deficit in HLA genetically confirmed by RFXANK mutation. Therefore, we concluded that for an HLA deficiency with IBD-like bowel disease and infectious cholangitis. The evolution was marked by the onset of acute febrile dyspnea with desaturation at 50, requiring intubation. Biology showed 350 elements/ mL lymphopenia with a positive CMV PCR: 86982 IU/ mL. Chest CT (Image 2) showed diffuse reticular-micronodular opacity with a positive search for pneumocystis jiroveci. A search for pneumocystis jiroveci was positive. The patient was put on ganciclovir and broad-spectrum antibiotics based on cephalosporines (ceftriaxone) and quinolones (levofloxacin), and immunoglobulin (tegelin). She passed away within 24 hours following a state of septic shock.

BELGIAN SOCIETY FOR GASTROINTESTINAL ENDOSCOPY (BSGIE)

- G01 -

REAL-TIME AUTOMATED ASSESSMENT OF HISTOLOGICAL DISEASE ACTIVITY IN PATIENTS WITH ULCERATIVE COLITIS USING SINGLE WAVELENGTH ENDOSCOPY TECHNOLOGY. P. Sinonquel (1), M. Lenfant (1), T. Eelbode (2), B. Callaerts (2), J. Guedelha Sabino (1), B. Verstockt (1), F. Maes (2), G. De Hertogh (3), S. Vermeire (1), R. Bisschops (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [2] KUL - University of Leuven, Leuven, Belgium, Electrical Engineering (ESAT/PSI), [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Pathology.

Introduction: Assessment of mucosal healing as a key denominator in the treat-to-target strategy for managing ulcerative colitis remains challenging. To address this, objective evaluation of histological disease activity holds promise. Recent offline research shows encouraging results using a new deep-learning convolutional neural network based on single wavelength endoscopy technology (SWE-CAD) (Fujifilm Co, Japan).
Aim: We aimed to validate the real-time performance of a new bedside prototype SWE-CAD model during standard colonoscopy.
Methods: A bedside module for real-time use was integrated in the endoscopy room to evaluate histological disease activity in patients with ulcerative colitis with Mayo Endoscopic Scoring (MES) ranging between 0 and 3. Imaging was performed in rectum and sigmoid following a standardized protocol based on white light and SWE (i.e. monochromatic light of 410nm). Biopsies were taken as reference at the center of the imaged region and were scored for the Geboes score (GBS). The SWE-CAD output was displayed on the separate monitor of the bedside module as a blue or red-colored indication, corresponding to histological remission or non-remission, respectively. Each region (2 in rectum and 2 in sigmoid) was simultaneously scored for MES by the endoscopist.
Results: In a total of 36 patients histological disease activity was automatically scored using the SWE-CAD. On a section level this CAD-system showed an accuracy of 96.4%, corresponding sensitivity was 99.3% and specificity was 85.5%. When differentiating for disease activity as mild, moderate and severe, accuracy was 97.7%, 62.8% and 95.0%, respectively. On a per-patient level, overall diagnostic accuracy remained high with 94.4%, with only 2/36 underestimations when compared to GBS.
Conclusions: In this pilot trial, we successfully tested a novel CAD-system, utilizing SWE technology, for real-time assessment of histological disease activity in patients with UC. The system demonstrated exceptional clinical accuracy at 94.4% per-patient level, potentially aiding physicians in interpreting subtle endoscopic abnormalities, leading to cost-effective and individualized patient management.

- G02 -

UNSEDATED OR ON-DEMAND MINIMALLY SEDATED WATER-AIDED OUTPATIENT COLONOSCOPY IN COLORECTAL CANCER SCREENING: A STEP FORWARD OR BACKWARD? EXPERIENCE FROM DAILY PRACTICE IN A REGIONAL (NON-ACADEMIC) HOSPITAL. S. Arnaert (1), D. Persyn (1), M. Cool (1), G. Lambrecht (1), G. Deboever (1) / [1] AZ Damiaan, Oostende, Belgium, Gastroenterology.

Introduction: The sedation levels and methods used for colonoscopy in colorectal cancer screening programs vary from country to country and from continent to continent. Although colonoscopies for colorectal cancer screening are considered non-complex procedures, they are increasingly performed under deep sedation and anesthesia usually with propofol and anesthesia monitored care (AMC). On the other hand, the interest in sedation-free and sedation on-demand colonoscopy is slowly growing due to better insertion techniques using dynamic position changes and water infusion instead of CO- insufflation.
Aim: We investigated whether the excellent results reported by expert endoscopists with water-aided unsedated colonoscopies are reproducible in daily practice in a regional (non-academic) hospital.
Methods: During the year 2023 (from January to October) 500 consecutive outpatients 50-75 years old presenting for colorectal cancer screening (abnormal fecal occult blood test in the national screening program, follow-up after previous polypectomy or suggestive symptoms) were informed about the possibility of unsedated or on-demand minimally sedated water-aided colonoscopy. 200 consecutive patients choosing for unsedated colonoscopy were included. During and after the procedure, data were collected (cecal intubation rate (CIR), adenoma detection rate (ADR), cecal intubation time (CIT), volume of water aspirated during the procedure, pain scores, use of Midazolam and willingness to repeat).
Results: 200 consecutive sedation-free or on-demand minimally sedated water-based colonoscopies were analysed. The total CIR was 98% (99% in men and 95% in women). The overall ADR was 65%; in the group with an abnormal fecal occult blood test the ADR was 75%. The mean CIT was 8.2 minutes (min), 7.6 min in men and 9.6 min in women (range 3.5-21 minutes). The mean aspirated volume of water during insertion was 360ml (range 100-1150 ml). Midazolam was administered in 4.5% of the patients (in 3.5% of men and in 7% of women). In men 5.7% of the procedures were experienced as moderate painful, and in women 11% (before administration of Midazolam), but none experienced severe

pain. The willingness to repeat future colonoscopies in the same way was 97% (98% in men and 95% in women). In addition, the efficiency of the day clinic was markedly improved: the median stay in the day clinic was 1 hour shorter than in colonoscopies performed under AMC.
Conclusions: Using water-aided insertion techniques and dynamic position changes, comfortable sedation-free or on-demand minimally sedated colonoscopy in daily practice in a regional hospital is feasible in the vast majority of patients presenting for colorectal cancer screening and the willingness to repeat future colonoscopies in the same way is very high.

- G03 -

IMPACT OF IMMERSIVE VIRTUAL REALITY DURING OUTPATIENT SEDATION-FREE COLONOSCOPY: A RANDOMIZED PROSPECTIVE CONTROLLED STUDY. M. Ayari (1), S. Riahi (1), I. Abdelaali (1), H. Douggui (1), T. Jomni (1) / [1] Internal Security Forces Hospital La Marsa, Tunis, Tunisia, Hepato-gastroenterology.

Introduction: Colonoscopy is the gold standard for accurate exploration of the colon. Thus, it must be performed as efficiently as possible while respecting pre-established quality standards to ensure optimal examination. The patient's tolerance considerably affects the quality of unsedated procedure and exposes to a high interruption rate. Pharmacological sedation can solve this issue, however, it can expose to significant adverse events and is not always available. Consequently, several studies have focused on non-pharmacological sedation options to optimize the good progress and quality of the colonoscopy.
Aim: The aim of this study was to evaluate the impact of intraprocedural immersive virtual reality (VR) combining visual and auditory distraction in the improvement of the tolerance and the progress during unsedated colonoscopy.
Methods: We conducted a prospective controlled study from February to April 2023 including outpatients presenting to the endoscopy unit for unsedated colonoscopy after consent. Patients were randomized into two groups: Group 1: colonoscopy with virtual reality headset. Group 2: control group without intervention. The material used was a virtual reality headset provided with a fully adjustable headband. The video content displayed on the hardware is made of several clips showing nature scenes. The audio content was adapted to allow optimal communication with the patient. We have excluded patients with severe visual and/or auditory impairment, dementia, cognitive impairment and epilepsy. All participants initially completed a form covering health issues and a validated anxiety questionnaire (STAI). After colonoscopy, all patients completed a form with questionnaires assessing per-procedural patient comfort (Gloucester), anxiety (STAI) and pain (EVS). In addition, patients in the intervention group completed a satisfaction questionnaire (NPS: net promoter score) assessing their experiences with the VR headset.
Results: In total, 63 patients were included in the final analysis: intervention group G1 (n=33) and control group G2 (n=30). The mean age was of 57 years. No patient encountered a technical problem with the equipment used and no adverse events occurred during the immersive experience. The two groups were comparable in terms of age, gender, comorbidities, body mass index (BMI) and colonic preparation assessed by the Boston score. A slightly lower time to caecal intubation was noted in the intervention group without significant difference (G1: 19 min vs G2: 26 min, p=0.07). Patients with VR mask expressed lower levels of post-procedural anxiety than those in the control group (Mean STAI G1: 47 vs G2: 53, $p<0.01$) and a significant decrease in the STAI score compared to pre-endoscopy values (8 points vs 4 points, $p<0.01$). The per-procedural pain assessed by EVS was significantly lower in the patients using VR (Mean G1: 0.44 vs G2:1.32, $p<0.01$). Moreover, endoscopic examination was found to be more comfortable with virtual reality based on the Gloucester scale $p<0.01$. No patient reported any impediment to communication with medical staff due to the VR mask. Four patients were not satisfied with the resolution of the videos and 8 patients have expressed their preference to choose the content themselves. Patients of the intervention group were greatly satisfied with the VR experience with a mean NPS at 30.
Conclusions: Immersive VR technology is a promising, non-invasive and well-accepted simple tool for improving tolerance by reducing colonoscopy induced pain and anxiety allowing an optimized examination. It can be a useful alternative to conventional sedation if undesired or contraindicated or in health care institutions with a lack of adequate anesthesia facilities.

- G04 -

THE AI-BASED RED DENSITY SCORE IS CORRELATED WITH THE ESTABLISHED AND NEW HISTOLOGICAL INDICES FOR ULCERATIVE COLITIS IN AN INDEPENDENT COHORT. P. Sinonquel (1), P. Bossuyt (2), S. John (3), M. Iacucci (4), U. Shivaji (5), H. Nakase (6), S. Van Aelst (7), S. Pillai (8), Z. Abdawn (9), S. Sugita (10), S. McCartney (11), A. Armuzzi (12), T. Bessissow (13), T. Rath (14), D. Yang (15), S. Vermeire (1), G. De Hertogh (16), R. Bisschops (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [2] Imelda Hospital, Bonheiden, Belgium, Gastroenterology and Hepatology, [3] Gold Coast Univerity Hospital, Gold Coast, Australia, Gastroenterology and Hepatology, [4] University College Cork, Cork, Ireland, Gastroenterology and Hepatology, [5] University of Birmingham, United Kingdom, Gastroenterology and Hepatology, [6] Sapporo Medical University, Sapporo, Japan, Gastroenterology and Hepatology, [7] Imelda Hospital, Bonheiden, Belgium, Pathology,

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Introduction: Red Density (RD) is an automated endoscopic tool that is developed for the objective evaluation of disease activity in ulcerative colitis (UC). Initial development was based on an algorithm including histological disease activity based on Robarts histological index (RHI). New histological scores for UC have been developed since.
Aim: To establish the correlation between RD and the Nancy histological index (NHI) and PICaSSO Histologic Remission Index (PHRI).
Methods: Patients included in 4 centers in the ongoing PROCEED-UC study (NCT04408703) had assessment with RD in the rectum and sigmoid at baseline, week 52 or early termination visit. RD score ranges between 0 and 255, cut-off for remission was previously determined to be <60.[1] Biopsies were taken according to protocol and scored for the Geboes score (GBS), RHI, NHI, PHRI in a blinded way after initial scoring convention training. Correlation was tested on patient level between mean RD per segment and the different histological indices based on Spearman correlation.
Results: Ninety-six patients from 4 centers were included representing 2634 RD images from 400 colonic segments with biopsies and corresponding RD score. Mean (± SEM) rectal RD score was 32.7 (± 4.54), 33.69 (± 5.25) and 64.86 (± 31.71) at baseline, w52 and ET, respectively. Mean sigmoidal RD score was 38.13 (± 3.68), 42.82 (± 11.80) and 77.33 (± 24.65) at baseline, w52 and ET, respectively. There was a significant correlation between the highest mean RD score per patient and the NHI ($r=0.60$, $p<0.0001$) and the PHRI ($r=0.62$, $p<0.0001$). In the rectum the RD score at all time points correlated significant with NHI ($r =0,53$, $p<0.0001$) and PHRI ($r=0.63$, $p<0.0001$). Similar correlation was seen in the sigmoid for NHI ($r=0.51$, $p<0.0001$) and PHRI ($r=0.22$, p0.0108). A RD score of <57.5 (AUC 0.7820 (95CI 0.7047 - 0.8593), $p<0.0001$) was associated with histological remission based on NHI (<2) and a RD score of < 64.5 (AUC 0.8133 (95%CI 0.7053 - 0.9212), $p<0.0001$) with histological remission based on PHRI (=0). The current dataset demonstrated to be stable in line with the previously established RD cut-off with GBS and RHI.[1]
Conclusions: In an independent cohort of patients with UC the correlation with the established and new histological indices is confirmed. This confirms the value of RD as objective endoscopic tool for the assessment of histological and endoscopic disease activity.
Reference: 1) Bossuyt P, Nakase H, Vermeire S, De G, Eelbode T, Ferrante M, et al. Automatic, computer-aided determination of endoscopic and histological inflammation in patients with mild to moderate ulcerative colitis based on red density. Gut. 2020;69:1778–86.

- G05 -

EVALUATION OF THE INCIDENCE OF POST COLONOSCOPY COLORECTAL CANCER IN A SPECIFIC PATIENT POPULATION BY USING A NEWLY DEVELOPED DASHBOARD FOR REAL-TIME AND ONGOING MONITORING OF PATIENT OUTCOMES AND ENDOSCOPIST PERFORMANCE.

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Introduction: Colorectal cancer (CRC) is a significant global health concern due to its high incidence rates and considerable impact on public health. Despite advances in screening and diagnosis, CRC remains a formidable adversary, claiming the lives of 2,520 people in Belgium in 2021. Colonoscopy allows for the identification and removal of polyps, reducing the risk of CRC development. However, even with the widespread use of colonoscopy, cases of CRC continue to arise following cancer-negative colonoscopies, a phenomenon referred to as post-colonoscopy CRC (PCCRC). Various factors influence the occurrence of PCCRC. Inadequate bowel preparation, as measured by the Boston Bowel Preparation Score (BBPS), and a short withdrawal time during colonoscopy are among the factors that have been associated with an elevated risk of PCCRC. Understanding these factors and their interactions is crucial for improving CRC screening and prevention strategies. The use of a POWERBI dashboard is a tool to collect data on screening colonscopies, including key performance indicators such as withdrawal time and adenoma detection ratio.
Aim: The primary objective of this study is to develop a comprehensive, integrated dashboard for in-depth analysis of PCCRC in our center. Secondary objectives are to analyze factors that contribute to the development of PCCRC in this specific patient population.

Methods: An integrated dashboard was meticulously designed and subsequently used for data analysis by anonymously and automatically retrieving coded data from the electronic patient records, including histopathological data, which were matched with the colonoscopic findings. A retrospective analysis was then performed to identify patients with a PCCRC and possible factors contributing to the development of PCCRC. PCCRC was defined as a cancer appearing up to ten years after a colonoscopy in which no cancer is diagnosed; according to the consensus statement published in Gastroenterology in 2018. Each case that did not meet PCCRC criteria underwent detailed manual review, resulting in their in- or exclusion from this study. The colonoscopy indications included for analysis were positive iFOBT, surveillance after adenomas and screening.
Results: The dashboard was developed by a data analyst under the guidance of the clinical nurse specialist in endoscopy and the gastroenterologists of our center. The initial version of this dashboard consists of the following data: demographics and comorbidities of the patients, number of colonoscopies and their indications, adenoma detection ratio per endoscopist, histopathology data coupled with the data from the endoscopy report, BBPS and withdrawal time. Using diagrams an easy overview of the current available data is readily visualised. From the 8930 screening colonoscopies performed between June 2019 and November 2023, 180 (2.02%) colorectal carcinomas were detected. 13/180 (7.2%) were PCCRC (6 males and 7 females). The median time to the detection of a PCCRC was 21 months (range 7 - 38). The median age of individuals diagnosed with PCCRC was 58 years (range 37 – 88). The median withdrawal time at the index colonoscopy was 8.5 minutes (range 6 - 54). The Boston Bowel Preparation Score (BBPS) was utilized to assess bowel preparation quality of the index colonoscopy, with a median score of 9 (range 5 - 9). The median adenoma detection ratio in our center is 48.1% (range 33.9% - 61.9%). Two patients died of PCCRC.
Conclusions: We identified and analyzed PCCRC cases by using a newly developed dashboard. This dashboard extracts coded data from patient files and allows for retrospective, real-time and ongoing monitoring. By using this tool as an audit, healthcare providers can take targeted actions to improve the quality of colonoscopies and aim to reduce the incidence of PCCRC. In the future, expansion of this dashboard should allow to extract data allowing for comparing groups and analyze risk factors associated with PCCRC. Ideally, a dashboard should be considered to be integrated in all endoscopy reporting systems providing real-time data on endoscopist's performance and patient outcomes.

- G06 -

LYMPHOVASCULAR INVASION IN THE SUBMUCOSA IS THE MAIN PREDICTOR OF LYMPH NODE INVOLVEMENT IN ENDOSCOPICALLY TREATED T1 COLORECTAL CANCER. N. Greiner (1), P. Baldin (2), H. Piessevaux (3) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Gastroenterology and hepatology, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Anatomopathology, [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Gastroenterology and hepatology.

Introduction: There is conflicting evidence whether the commonly used risk factors for recurrence after local resection of early colorectal cancer are equally important. For example, a Dutch meta-analysis reported the low importance of the depth of submucosal infiltration in this setting (Zwager, 2022). On the other hand, a Japanese national cohort was recently used to design a nomogram, but in their hands, submucosal depth of infiltration is of great importance (Kajiwara, 2023).
Aim: The aim of the present study was to evaluate the predictors of lymph node metastasis in our large monocentric cohort of 802 colorectal ESD's with very long follow-up.
Methods: We queried our prospectively completed database of colorectal ESD performed at our institution, to identify all patients with pT1 sm+ adenocarcinoma. This database contains, demographic, diagnostic endoscopy (location, polyp classification), therapeutic endoscopy (technique, complications) data, pathology results as well as additional surgery results (if performed), and the patients' clinical and endoscopic follow-up.
Results: We identified 81 patients with pT1 sm+ adenocarcinoma (46 male, mean age 69.2±10.3). Median follow-up time was 40 months, range 0-14 years. Thirty-five patients (43.2%) underwent surgical resection with lymphadenectomy, while 45 (55.5%) were followed-up, either because there was no indication for surgery (26/45 ; 57.8%) or because of patients preferences or comorbidities (19/45 ; 42.2%). As expected, patients of the follow-up group were older (mean age 70.6 versus 65.5 years). In the surgery group, 4 patients had lymph node metastasis (LNM) on the resection specimen (11%): all of them had lympho-vascular invasion (LVI) on the ESD specimen, 3 had also deep submucosal invasion (DSI), 1 had high-grade tumor budding. None of the 19 patients with DSI as only risk factor had LNM. In the follow-up group, no patient experienced nodal or metastatic recurrence. Four (8.8%) had local recurrence: all of them had DSI, 3 had undergone piecemeal resection because of failed ESD, 2 had positive margins. Nine patients of this group had DSI as only risk factor for LNM.
Conclusions: LVI is the main predictor of lymph node involvement in endoscopically treated T1 CRC. DSI is not a strong risk factor for LNM, and should in se not be considered an indication for additional surgery in the absence of other risk factors.

- G07 -

VIDEO ASSESSMENT OF LARGE NON-PEDUNCULATED COLORECTAL POLYPS SIMILARLY PREDICTS HARD OUTCOMES IN THE ASSESSMENT OF SUBMUCOSAL INVASIVE CANCER RISK COMPARED TO

LIVE ASSESSMENT. M. Montori (1), S. Ridolfo (2), P. Poortmans (3), S. Smeets (2), M. Argenziano (2), T. Tornai (2), L. Debels (2), L. Desomer (2), D. Tate (2) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastrointestinal and liver diseases, [2] University Hospital Ghent (UZ Gent), Gent, Belgium, Maag-, darm- en leverziekten, [3] UZ Brussel, Brussels, Belgium, Gastroenterology.

Introduction: Cancer in large non-pedunculated colorectal polyps (LNPCPs) is poorly discriminated outside expert centres. It is unknown whether video-assessment is comparable to live assessment in its accuracy of determining SMI in LNPCPs. Video-assessment has multiple advantages including allowing multiple assessors who may be remote and not able to attend at the time an LNPCP is detected to collaboratively discuss imaging findings at multi-disciplinary meetings. This may allow for rapid standard-of-care treatment selection for patients without them having to undergo a further assessment procedure by a specialist.
Aim: We aimed to compare live assessment of LNPCPs with analysis of high-quality endoscopic videos produced by an expert.
Methods: Eighteen live assessments of LNPCPs from consecutive, consenting patients were conducted by 15 endoscopists in a single center. Each endoscopist independently evaluated the LNPCPs blinded to others' assessments. After the live assessment, an expert recorded a standardized video of each LNPCP (paused overview high-definition white light [HDWL], HDWL assessment 20s, magnified HDWL 20s, virtual chromoendoscopy [VC] overview 20s and magnified VC 20s). Endoscopists [who had not assessed the LNPCP live] assessed these videos using an online survey format at a later date. Parameters such as Blink Impression (BI), 6-Blink Features (BF) – namely fold deformation, extra redness, depression, chicken skin mucosa, ulceration and spontaneous bleeding, presence of a Demarcated Area (DA), Vascular Pattern (VP) of any DA, size, location, Paris classification, and morphology were recorded to form the endoscopists' impression of cancer presence in the LNPCP. The results were later compared to expert opinion derived from a consensus meeting involving the lead author and an external expert validator, conducted more than four weeks after the final polyp assessment. The primary endpoint was to evaluate the accuracy of endoscopists' final impression of cancer andetermination of correct treatment between live and video assessments, with secondary endpoints including the accuracy of feature detection and treatment recommendations.
Results: A total of 18 LNPCPs were assessed live by 12 endoscopists and 13 were video-assessed by 8 endoscopists. Experience of the assessors was stable between video and live assessments (live: 6/12 (50%) < 50 EMRs, 5/12 (41.7%) <1000 colonoscopies, video: 4/8 (50%) and 3/8 (37.5%) respectively). The comparison of live versus video assessments revealed no statistically significant difference in the final impression of cancer presence by the endoscopist, (sensitivity 80.0% vs 100.0%, specificity 87.0% vs 85.5%, accuracy 85.9% vs 87.5%), BI vs. histology (sensitivity 85.7% vs 92.3%, specificity 88.6% vs 80.7%, accuracy 88.2% vs 82.3%), and the presence of at least 2 BF (sensitivity 71.4% vs 84.6%, specificity 81.8% vs 68.7%, accuracy 80.4% vs 70.8%, P-values: 1, 0.763, and 0.814, respectively). Additionally, the ability of DA and JNET to predict submucosal invasion (SMI) did not differ (P=1.000 and 0.934 respectively) nor did the rate of correct treatment determination (71.9% live vs 60.4% video, P=0.187). When considering comparisons with expert assessment the determination of ≥2 BF showed a significant difference between live and video assessments (live accuracy 82.4%, video accuracy 76.0%, P=0.019). Similarly, the sum of blink features differed significantly (exact match: live 60.8%, video 37.5%, P=0.012). The presence of three or more features (location, size, morphology, and Paris classification) of COVERT (not visible on the surface) SMI, when compared with experts, differed significantly between live and video assessments (live 81.3%, video 65.6%, P=0.048). The correct outcome of a structured algorithm [1] compared with that determined by expert consensus, was significantly different between live and video assessments (live 96.9%, video 81.3%, P=0.007).
Conclusions: Final impression of the presence of cancer and determination of correct treatment in LNPCPs are predicted equally well from blinded video assessment versus live assessment in a group of similarly experienced endoscopists. Live assessment did improve reporting of detailed features versus expert opinion. If replicated in larger studies this finding suggests that structured video can be safely and effectively used to interpret the risk of SMI in LNPCPs and therefore determine treatment at a time remote from the detecting procedure. This could minimise the need for patients to undergo a repeat procedure to assess their LNPCP prior to resection.

- G08 -

IMPACT OF A NEW ELECTRONIC PATIENT RECORD AND THE INTRODUCTION OF A CLINICAL NURSE SPECIALIST ENDOSCOPY ON ADENOMA DETECTION RATES. S. Corneillie (1), F. Marolleau (2), F. Baert (2), L. Baert (2), S. De Meulder (2), F. De Pauw (2), C. De Vloo (2), J. Dewyspelaere (2), L. Harlet (2), P. Vandecandelaere (2), J. Bossuyt (3), F. Dedeurwaerdere (4), J. Decaestecker (2), L. Desomer (2), D. Dewulf (2) / [1] AZ Delta, Roeselare, Belgium, Endoscopie, [2] AZ Delta, Belgium, Department of Gastroenterology and Hepatology, [3] AZ Delta, Belgium, Data-Analysis Oncology, [4] AZ Delta, Belgium, Department of Histopathology.

Introduction: Colorectal cancer screening, particularly through colonoscopy, is a pivotal element of preventive healthcare. Understanding the multifaceted factors influencing Adenoma Detection Rates (ADR) is crucial for optimizing

the effectiveness of screening programs. This study aims to provide a detailed analysis of the impact of electronic patient records, clinical interventions, and other variables on ADR trends in a gastroenterology unit.
Aim: This study aims to investigate the factors contributing to the increase in ADR over time through the implementation of a comprehensive colonoscopy Quality Indicator recording system.
Methods: This study investigates the trends in Adenoma Detection Rates (ADR) and associated factors in a single center gastroenterology unit over a four-year period. The primary outcome is the evolution of ADR, with secondary outcomes including the relationship between ADR and withdrawal time, endoscopists' experience, and the Boston Bowel Preparation Scale (BBPS). The introduction of a new electronic patient record in 2019 establishes the baseline for data analysis. In 2022, a full-time clinical nurse specialist in endoscopy began actively monitoring key indicators, such as ADR, BBPS, and withdrawal time. These metrics were regularly communicated to endoscopists through a PowerBi dashboard. As part of clinical interventions, a patient preparation video was introduced to enhance communication and standardize information for patients undergoing colonoscopies.
Results: We included patients aged 50 or older, with a total of 3340 colonoscopies performed between January 2019 and September 2023. 8000 colonoscopies are performed per year, but we only include the adenoma screening indications. The analysis revealed a significant increase in ADR in 2020, coinciding with the introduction of electronic patient records. This marked rise, at 13.5%, suggests a positive influence of improved record-keeping on diagnostic accuracy. However, subsequent years showed a more modest increase of 0.4%, indicating a potential plateau effect. In 2022, the introduction of a full-time clinical nurse specialist in endoscopy corresponded with changes in key indicators. The BBPS showed a significant decrease in 2023 compared to 2022 ($p=0.03$), while a reverse trend was observed between 2020 and 2021 ($p = 0.03$). Endoscopist's experience ($p= 0,2470$), and BBPS scores ($p= 0,1652$) were no significant predictors of the increased ADR. Adjusted for the other variables included in the model. These findings underscore the complex interplay of various factors influencing procedural outcomes.
Conclusions: The dynamic nature of ADR observed in this study prompts a closer examination of the long-term effects of electronic patient records on diagnostic accuracy. The initial surge in ADR following their introduction suggests a positive and immediate impact on procedural outcomes. However, the subsequent stabilization of ADR raises questions about the sustainability of this effect over time. The introduction of a full-time clinical nurse specialist in endoscopy in 2022 may have contributed to the observed changes in BBPS. This emphasizes the potential benefits of multidisciplinary collaboration in optimizing colonoscopy outcomes. The observed decrease in BBPS in 2023, coupled with the sustained ADR levels, suggests a need for ongoing assessment of clinical interventions. The patient preparation video, introduced as part of enhanced communication strategies, may have contributed to these changes. Future research should delve deeper into the nuanced impact of such interventions on procedural outcomes and patient experiences.

- G09 -

SURGERY VERSUS ENDOSCOPIC THERAPY FOR MIRIZZI SYNDROME (SEIZE)-STUDY: A MULTICENTRE INTERNATIONAL EXPERIENCE. J. Tengan (1), M. Bronswijk (2), L. Aldrighetti (3), P. Arcidiacono (4), M. Bruno (5), F. Cipriani (3), J. Dhar (6), S. Everett (7), C. Gerges (8), J. Gauci (7), V. Gupta (6), M. Hollenbach (9), G. Johnson (10), S. Lakhtakia (11), W. Laleman (1), W. Lammers (5), A. Lemmers (12), J. Omoshoro-Jones (13), S. Ouazzani (14), A. Papaefthymiou (10), E. Pérez-Cuadrado-Robles (15), F. Prat (16), G. Rahe (17), N. Reddy (11), G. Saelman (18), J. Samanta (6), G. Vanella (19), K. Vermeiren (20), J. Vila (21), H. van Malenstein (1), A. Waldthaler (22), R. van Wanrooij (23), B. Zonderhuis (18), R. Kunda (24), G. Webster (10), S. van der Merwe (25) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] Imelda Hospital, Bonheiden, Belgium, Department of Gastroenterology and Hepatology, [3] Vita Salute San Raffaele University, Milan, Italy, Hepatobiliary Surgery Division, [4] Vita Salute San Raffaele University, Milan, Italy, Pancreatobiliary Endoscopy and Endosonography Division, Pancreas Translational and Clinical Research Center, [5] Erasmus MC, University Medical Center Rotterdam, The Netherlands, Department of Gastroenterology and Hepatology, [6] Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India, Departments of Gastroenterology and GI Surgery, [7] Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom, Department of Gastroenterology, [8] University Hospital Essen, Essen, Germany, Department of Gastroenterology, [9] University of Leipzig Medical Center, Leipzig, Germany, Division of Gastroenterology, Medical Department II, [10] University College London Hospitals NHS Foundation Trust, London, United Kingdom, Pancreatobiliary Medicine Unit, [11] Asian Institute of Gastroenterology, Hyderabad, India, Asian Institute, [12] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, [13] Chris Hani-Baragwanath Academic Hospital, Johannesburg, South Africa, Department of Surgery, [14] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Gastroenterology, [15] Georges-Pompidou European Hospital, APHP. Centre, University of Paris Cité, Paris, France, Department of Gastroenterology, [16] Hôpital Cochin (AP-HP), Paris, France, Gastroenterology Unit, [17] University Hospital Essen, Essen, Germany, Department of Gastroenterology, [18] Amsterdam UMC, Amsterdam, The Netherlands, Department of Surgery, [19] Vita Salute San Raffaele University, Milan, Italy, Pancreatobiliary Endoscopy and Endosonography Division, [20] Imelda General Hospital, , Belgium, Department of General and Abdominal Surgery, [21] Servicio de Aparato Digestivo, Complejo Hospitalario de Navarra, Pamplona, Spain, Unidad de Endoscopia, [22] Karolinska Institutet, Karolinska University Hospital, Sweden, Department of

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Introduction: The management of Mirizzi syndrome has been primarily surgical, ranging from cholecystectomy to en bloc resection with hepatico-jejunostomy for advanced Csendes III and IV types. The introduction of digital single-operator cholangioscopy (dSOC) allows for ductal clearance in patients with Mirizzi syndrome. Although small series have highlighted the feasibility of an endoscopic approach, there is a lack of comprehensive comparisons between surgical and endoscopic treatments.
Aim: The objective of the current study is to compare the outcomes and safety of dSOC-guided lithotripsy with the surgical approach.
Methods: A large multicenter international retrospective analysis was conducted on dSOC and surgical procedures in patients with type II-IV Mirizzi syndrome between January 2005 and June 2022. Patients with postsurgical anatomy, Mirizzi type I, or a history of pre-dSOC cholecystectomy were excluded. Technical success was defined as the successful and complete clearance of the duct using either dSOC or surgery. The AGREE classification was employed for adverse event (AE) grading.
Results: In total, 290 patients were included, with 176 undergoing treatment with dSOC and 114 undergoing surgery. At baseline, patients undergoing dSOC were older (61.3 years [SD16.4] vs. 56.0 [SD14.8]), experienced jaundice more frequently (79.4% vs. 61.9%, p=0.001), and had higher scores on the Charlson Comorbidity Index (3 [IQR 1-9] vs. 1 [0-3], p<0.001) and ASA scores (p<0.001). While technical success was lower in the dSOC group compared to surgery (89.2% vs. 96.5%, p=0.025), the need for reinterventions and the median number of interventions were similar after a median follow-up duration of 741.5 days (IQR 320-1781) vs. 346 (IQR 67-1220) days (p=0.009). Overall adverse events (AE) occurred less frequently in the dSOC group (10.2% vs. 41.2%, p<0.001), including mild AE (4.0% vs. 13.1%, p=0.008), and severe AE (1.7% vs. 15.8%, p<0.001). Three fatal complications occurred in the surgical group (0.0% vs. 2.6%, p=0.060). During follow-up, cholecystectomy was avoided in 115 out of 175 dSOC patients (65.3%), without resulting in statistically significant differences in long-term outcomes. When comparing patients from the primary surgery group with patients in whom elective cholecystectomy following dSOC was performed, a lower need for hepaticojejunostomy was observed (6.6% vs. 26.1%, p=0.002).
Conclusions: Our study demonstrates that the use of dSOC for the removal of intraductal stones in Mirizzi syndrome is highly effective, showing superior safety despite treating patients with more underlying comorbidity. Digital single-operator cholangioscopy may prevent the need for subsequent cholecystectomy in two-thirds of patients and, if still required, downgrade the extent of surgery to a cholecystectomy with primary repair, potentially reducing the need for a hepaticojejunostomy. Consequently, we advocate for dSOC as the primary modality in the management of Mirizzi syndrome

- G10 -

SINGLE-SESSION EUS-DIRECTED TRANSGASTRIC ERCP WITH A DEDICATED OVER-THE-SCOPE FIXATION DEVICE: A FEASIBILITY STUDY. M. Bronswijk (1), S. van der Merwe (2) / [1] Imelda Hospital, Bonheiden, Belgium, Department of Gastroenterology and Hepatology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: EUS-directed Transgastric ERCP (EDGE) has been proposed as a more effective alternative to enteroscopy-assisted ERCP for patients with Roux-en-Y gastric bypass anatomy, overcoming the invasiveness of laparoscopy-assisted ERCP. Postponing through-the-LAMS ERCP for 1-2 weeks and employing stent fixation techniques have been suggested to reduce the risk of stent migration.
Aim: Our aim is to investigate the feasibility of a single-session EDGE using a dedicated over-the-scope fixation device.
Methods: A tertiary single-center retrospective analysis of prospectively collected data was conducted on all consecutive single-session EDGE procedures performed with the dedicated Stentfix device (Ovesco Endoscopy AG, Tuebingen, Germany). Only 20x10mm LAMS were utilized, and all cases between September 2022 and October 2023 were included. The primary outcome was LAMS migration, while key secondary outcomes included adverse events (of any kind) and technical success, defined as the successful achievement of through-the-LAMS ampullary access during a single session using a duodenoscope. Adverse events were graded using the AGREE classification.
Results: Eleven patients were identified, with a mean age of 56 years (SD±11.7), and a female predominance of 63.6%. All patients had classic Roux-en-Y gastric bypass anatomy and underwent ERCP for various reasons: bile duct stones (n=7, 63.6%), cholangitis (n=2, 18.2%), and post-cholecystectomy leaks (n=2, 18.2%). No LAMS migrations occurred, and technical success was achieved in 10 out of 11 patients (90.9%). After a median follow-up time of 97 days (IQR 29-231), one adverse event (grade I) was reported, involving postprocedural pain which resolved following administration of mild opioid analgesia and subsequent removal of the stent. The median procedure time was 45 minutes (IQR 41-51). The median LAMS dwell time was 29 days (IQR 21-53), and the majority of fistulae (75%) were closed immediately

after LAMS removal, using an over-the-scope clip. The median body mass change during LAMS implantation was +2kg (IQR 0-2).
Conclusions: While acknowledging that factors such as the endoscopist's experience, LAMS orientation, and a larger stent size (20mm vs 15mm) cannot be definitively excluded as contributing elements, our data strongly suggest that the utilization of a dedicated over-the-scope stent fixation device prevents LAMS migration during the same-session EDGE

- G11 -

ENTEROSCOPY-ASSISTED ERCP VERSUS EUS-ANTEGRADE TREATMENT OF STONES AND/OR STRICTURES IN PATIENTS WITH ROUX-EN-Y HEPATICOJEJUNOSTOMY: A TERTIARY CENTER COMPARISON. M. Bronswijk (1), A. van Oosterwyck (2), T. Ogura (3), S. van der Merwe (2) / [1] Imelda Hospital, Bonheiden, Belgium, Department of Gastroenterology and Hepatology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [3] Osaka Medical College, Osaka, Japan, 2nd Department of Internal Medicine.

Introduction: Bile duct access in patients with surgically altered anatomy poses a clinical challenge to the interventional endoscopist. Although PTC and enteroscopy-assisted ERCP (e-ERCP) are often preferred for patients with hepaticojejunostomy (HJ) and Roux-en-Y reconstruction, these approaches are plagued by either relatively high morbidity or suboptimal effectiveness respectively. EUS-guided antegrade treatment of HJ strictures and/or stones has been suggested as a safe and effective alternative by creating an easily re-accessible portal to the biliary tree, although limited comparative data are available.
Aim: Our aim is to compare EUS-guided antegrade treatment with e-ERCP for HJ strictures and/or stones.
Methods: A tertiary single-center retrospective analysis was performed of all consecutive EUS-antegrade procedures in patients with hepaticojejunostomy and Roux-en-Y reconstruction from October 2019 to May 2023. Patients with actively underlying malignancy, Billroth-II reconstruction, Roux-en-Y gastric bypass or a naïve papilla were excluded. EUS procedures were performed using EUS-guided hepaticogastrostomy with fully-covered SEMS placement (fc-SEMS) at the index procedure, followed by SEMS extraction and antegrade treatment using balloon dilation with or without Spyglass from subsequent procedures onwards. The primary outcome was technical success, defined as the successful completion of desired steps with stricture dilation and/or stone removal with subsequent stenting. Secondary outcomes were adverse events and procedure duration. Adverse events were graded based on the AGREE classification.
Results: Thirty-five patients were included, of which 16 were treated with EUS-antegrade treatment and 19 had undergone e-ERCP. In both groups, the majority of patients had a history of pancreatoduodenectomy with Roux-en-Y hepaticojejunostomy (68.8% vs. 79%, p=0.700). Technical success was similar in both groups (87.5% vs. 73.7%, p=0.415), with two failures in the EUS group due to insufficient bile duct dilation and five failures in the e-ERCP group due to inability to cannulate the HJ (n=2) or access the afferent limb (n=3). Overall adverse event rates were similar (4 [25%] vs. 2 [10%], p=0.379), with two grade I (pain) complications occurring in the EUS group and two grade II (cholangitis) in the e-ERCP group. The only grade IIIa adverse event was detected in the EUS group, due to post-procedural abdominal pain which required endoscopic re-evaluation. Index procedure duration was significantly shorter in the EUS group (46 [31-60] vs. 72 [IQR 41-98] minutes, p=0.016), whereas hospital stay was similar (7.5 [1-12] vs. 1 [1-7] days, p=0.347). After a median follow-up of 448 days (IQR 164-644) vs. 694 days (IQR 236-1288, p= 0.204), a numerical difference in recurrence rates was seen (1 [6.3%] vs. 4 [21.1%], p=0.347), based on restenosis in all cases. As expected due to preplanned reinterventions, more reinterventions were performed in the EUS group (3 [IQR 0-4] vs. 0 [0-2] procedures, p=0.021).
Conclusions: Our data suggest that EUS-antegrade treatment is equally safe and effective when compared to e-ERCP in patients with Roux-en-Y hepaticojejunostomy, with the advantage of resulting in lower procedure time and facilitating easier biliary re-access as well as guiding digital single-operator cholangioscopy if required. EUS-antegrade treatment should be regarded as a valuable complementary addition to our endoscopic armamentarium in patients with postsurgical anatomy.

- G12 -

PERFORMANCE OF LAMS FOR ANASTOMOSIS CREATION BETWEEN TWO SEGMENTS OF THE GASTROINTESTINAL TRACT: A LARGE SINGLE-CENTRE EXPERIENCE. E. Gökce (1), P. Hindryckx (1) / [1] University Hospital of Ghent, Belgium, Gastroenteroly and Hepatology.

Introduction: In the last few years, lumen-apposing metal stents (LAMSs) have been used for off-label indications, including the creation of an anastomosis in the gastrointestinal (GI) tracts such as endoscopic ultrasound-guided gastro-gastrostomy (EUS-GG), gastro-enterostomy (EUS-GJ) and entero-enterostomy (EUS-EE). Indications include a) a need for access to excluded parts of the GI tract in patients with surgically altered anatomy, b) alleviation of gastric outlet obstruction (GOO) and c) treatment of a number of specific conditions (eg. afferent limb syndrome, bypass breakdown…).

Aim: The aim of this study was to evaluate the performance of LAMS for anastomosis creation between two segments of the GI tract.
Methods: All consecutive patients who underwent EUS-GG, EUS-GE or EUS-EE between October 2019 and November 2023 were included in this analysis. The main outcome data of interest were technical success, clinical success and adverse events. Technical success was defined as a successful placement of LAMS in the desired position. Clinical success was defined as either successful endoscopic access to the intended excluded GI segment in patients with surgically altered anatomy, or successful re-initiation of oral food intake in patients with GOO, or achievement of the intended therapeutic goal for the remaining specific conditions. Adverse events were classified according to the AGREE criteria and grouped into minor (AGREE I and II) and major adverse events (AGREE IIIa, IIIb, and IV).
Results: A total of 127 LAMS were placed in 119 patients (mean age, 61 years; 63% women) to create a GG, GE or EE anastomosis. The overall technical and clinical success rate was very high [124/127 (97.6 %) and 118/125 (95.0%), respectively]. Adverse events were seen in 18/127 cases [14.2%; 10/18 (55.6%) minor, 8/18 (44.4%) major]. Fifty-seven procedures (44.9%) were performed in 54 patients (mean age, 54 years; 74% women) to create access to an excluded part of the GI tract. The technical and clinical success rates were 55/57 (96.4%) and 53/55 (96.2%), respectively. The most common indication (54/57, 94.7%) was the need for endoscopic access to the excluded stomach or duodenum in patients with a Roux-en-Y gastric bypass. In 3 (5.3%) cases, an anastomosis between the duodenum and the afferent limb was created to obtain easy access to a hepaticojejunostomy. A 20/10 mm LAMS was used in 51/57 (89.5%) cases, and a 15/10 mm LAMS in 6/57 (10.5%) cases. The LAMS was fixated with clips in 31/57 (54.4%) cases and dilatation of the LAMS lumen was performed in 21/57 (36.8%). A single-session procedure (anastomosis creation + endoscopic intubation of the target) was performed in 23.6%. In the other cases, the mean time between LAMS placement and the needed endoscopic procedure was 16 days [range 6-94]. The LAMS was removed in 51/57 (89.4%) cases after a mean time of 71 days [range 7-431]. Adverse events were seen in 10/57 (17.5%), of which 4/10 were severe [stent migration needing surgery (N=1), 2/55 persisting fistula needing endoscopy (N=1) and surgery (N=1), and respiratory desaturation, needing observation on an intensive care unit (N=1]. There was no procedure-related mortality. Sixty-one EUS-GJ procedures were performed in 57 patients (mean age, 67 years; 53% women) for alleviation of GOO. Forty-five patients (71.9%) had malignant GOO (mGOO) and 16/57 (28.0%) had benign GOO (bGOO). The technical and clinical success rates were similar in both subgroups [44/45 (97.8%) and 44/44 (100%) in mGOO; 16/16 (100%) and 15/16 (93.8%) in bGOO, respectively]. A 20/10 mm LAMS was used in all patients. The LAMS was fixated with clips in 32/61 (52.5%) cases and dilatation of the LAMS lumen was performed in 32/61 (52.5%). The LAMS was removed in only 5/61 (8.2%) of the mGOO (2/47 (4.4%) and 3/16 (18.8%) of the bGOO cases). Adverse events were seen in 7/61 (11.5%), of which 3/7 were severe [bleeding (N=2) and a refractory enterocolonic fistula (N=1), all needing an endoscopic reintervention]. Loss of LAMS patency occurred in 3/61 cases (4.9%) after a mean interval of 247 days [range 39-592]; two were endoscopically cleaned, and in one case a new LAMS was placed. There was no procedure-related mortality. Nine procedures were performed in eight patients (mean age, 65 years; 89% women) with a specific therapeutic purpose (refractory stenosis of gastro-jejunostomy; undo of RYGB in patients with malignant cachexia; afferent limb syndrome; and endoscopic pyloric exclusion). The technical and clinical success rates were 9/9 (100%) and 6/9 (75%), respectively. A 20/10 mm LAMS was used in all patients. The LAMS was fixated with clips in 5/9 (55.6%) cases and the LAMS lumen was dilated in 4/9 (44.4%). The LAMS was removed in 4/9 (44.4%) cases after a mean time of 51 days [range 27-89]. In 1/9 (11.1%) of the cases, an iatrogenic ulcer bleeding occurred, needing endoscopic hemostasis. There was no procedure-related mortality.
Conclusions: Creation of an anastomosis between two segments of the GI tract with a LAMS is effective, with an acceptable risk of procedure-related adverse events. The procedure offers a minimally invasive option to A: gain easy access to excluded parts of the GI tract in patients with a surgically altered anatomy and B: alleviate malignant and benign GOO.

- G13 -

FACTORS ASSOCIATED WITH THE SEVERITY OF ERCP-RELATED COMPLICATIONS: LARGE RETROSPECTIVE MONOCENTRIC STUDY. K. Goubert (1), P. Hindryckx (1) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology.

Introduction: Prospective studies have identified a number of patient- and procedure-related risk factors for post-ERCP complications. Many of these complications are mild and self-limiting.
Aim: The aim of this study is to identify the patients at risk for severe post-ERCP complications.
Methods: All patients with post-ERCP complications within 30 days after ERCP between January 2016 and December 2022 were identified based on a prospectively collected ERCP registry. A 29-variable dataset was built based on prospectively collected data and retrospective analysis of the patient records. The severity of the complication was graded according to the AGREE-criteria. Severe complications were defined as AGREE > 2. Univariate and multivariate regression analysis was performed to identify factors associated with severe post-ERCP complications.
Results: A total of 2810 ERCP procedures were performed, of which 223 (7.9%) led to a post-ERCP complication. The median age within this subpopulation was 68 (IQR 54 to 76) and 136 patiënts (61%) had major comorbidities (defined as ASA≥3). The most commonly described complication was pancreatitis (82 cases, 37%), followed by hemorrhage (70

cases, 31%), infectious complications (55 cases, 25%), perforation (15 cases, 7%) and MOF (1 case, 0.4%). 6 patients died <30 days after the ERCP procedure; 6/223 (2.7%) complications resulted in death. With regard to severity of the post-ERCP complication, 174/223 (78%) cases were classified as "non-severe" [128 AGREE 1 (57%); 46 AGREE 2 21%)] and 49/223 (22%) were classified as "severe" [31 AGREE 3 (14%); 12 cases AGREE 4 , (5%) and 6 cases AGREE 5 (3%)]. Hemorrhage was the most reported severe complication (22/49 severe complications, 44.9%), while a perforation had the most chance to result in a severe complication (10/15 perforation cases, 67%). Univariate analysis identified 2 patient-related variables (anticoagulative therapy and age) and 2 procedure-related variables (difficulty of ERCP, defined by Shutz III or IV and incomplete biliary drainage) associated with severe post-ERCP complications. Multivariate analysis withheld anticoagulative therapy (OR 6.3, 95% CI 1.4-28.3, P= 0,016) and a difficult ERCP defined by Schutz III (OR 11.5, 95% CI 2.4-54.6, P= 0,002) or IV (OR 5.9, 95% CI 1.4 to 23.5, P= 0,012) as independent risk factors for a severe post-ERCP complication.
Conclusions: Patients under anticoagulant therapy and patients undergoing difficult ERCP procedures (Schutz III or IV) have the highest risk of a severe post-ERCP complication.

- G14 -

BALLOON DILATION-ASSISTED EXTRACTION OF EMBEDDED BILIARY SELF-EXPANDABLE METAL STENTS: A PROOF-OF-CONCEPT STUDY. M. Bronswijk (1), A. Reekmans (2), S. Van der Merwe (3) / [1] Imelda Hospital, Bonheiden, Belgium, Department of Gastroenterology and Hepatology, [2] ASZ, Aalst, Belgium, Gastroenterology and Hepatology, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology.

Introduction: Embedded transpapillary self-expandable metal stents (SEMS) often lead to obstructive biliary complications. Endoscopic extraction is generally required and standard approaches often fail. In the current study we describe a newly developed approach to treating refractory embedded SEMS, using balloon dilation-assisted stent extraction or 'BASE'.
Aim: Our aim was to evaluate the feasibility and outcomes of this technique.
Methods: This is an exploratory single-center retrospective analysis and all consecutive patients undergoing endoscopic balloon-assisted stent extraction were included. During this procedure, a 15mm through-the-scope dilation balloon is inflated in the embedded SEMS and distal bile duct, after which the SEMS and dilation device are both extracted simultaneously by firm continuous traction. Baseline, procedural and follow-up data were collected and analyzed. The AGREE-classification was used for adverse event grading.
Results: Twelve patients with embedded transpapillary SEMS were identified (60.0% female, mean age 70.1 [SD±18.1] years, uncovered SEMS 33.3%) with median SEMS dwell time of 457.5 (IQR 175.8-1042) days. Previous extraction attempts were undertaken in the majority of cases (83.3%), including forceps traction (58.3%) and SEMS-in-SEMS placement (41.7%). Using the balloon-assisted stent extraction or 'BASE' technique, successful SEMS extraction was achieved in 10 out of 12 cases (83.3%). Adverse events occurred in 2 patients (Grade I [n=1, 8.3%] - Grade II [n=1, 8.3%]), consisting both of immediate postprocedure episodes of cholangitis, which were both treated successfully with antibiotics. After a median follow-up time of 171 (58-260) days, 1 biliary re-obstruction occurred for which endoscopic re-evaluation and a negative balloon sweep was performed.
Conclusions: Our data suggest that endoscopic balloon-assisted stent extraction or 'BASE' can be considered for extraction of embedded self-expandable metal stents, as it showed high efficacy without any major procedure-related adverse events, using readily available endoscopic tools.

- G15 -

PERORAL ENDOSCOPIC MYOTOMY: A TWO-CENTER RETROSPECTIVE STUDY OF PRACTICE AND ADVERSE EVENTS. C. Van Severen (1), J. Loly (2), M. Poncin (2) / [1] Liege University Hospital, Liege, Belgium, gastroenterology and endoscopy, [2] Liege University Hospital, Liege, Belgium, gastroenterology and endoscopy.

Introduction: Peroral endoscopic myotomy (POEM) is an endoscopic technique of esophageal myotomy indicated in the treatment of esophageal motility disorders, and mainly, in achalasia. It is less invasive than surgery and has comparable functional results. Serious complications from POEM are rare. The most common intra- and perioperative adverse events are pain, bleeding, perforation, infection, and insufflation-related side effects. Most of these adverse events can be treated during the operative procedure or managed conservatively. The most belated adverse event is GERD. For the past decade, POEM has been recognized as an effective and safe endoscopic technique for the treatment of achalasia. This study was performed to compare two university centers in the practice of peroral endoscopic myotomy (POEM) in terms of efficacy and adverse events, for the treatment of esophageal motility disorder.
Aim: The primary objective is to evaluate the practice of POEM as a treatment for esophageal motility disorders, in terms of efficacy and adverse events, and to compare the results between two university centers: the Regional University Hospital Center of Besançon (France) and the University Hospital Center of Liège (Belgium). The clinical success is

evaluated using a score, the Eckardt symptom score (the treatment being considered effective if this score is ≤ 3). This primary end point includes minor adverse events (complications of the procedure that can be treated during the operative procedure or managed conservatively) and major adverse events (complications of the procedure that led to the need of revision surgery, admission to the intensive care unit or death). The main aim is also to study the impact of the level of expertise between the two centers, with the French center using this technique for eight years and the Belgian center for three years. The secondary objective is to study intraoperative and perioperative factors as potential predictors of postoperative pain and/or adverse event.
Methods: This is a retrospective, observational, bicentric study. It includes fifty-five patients treated with POEM from September 2020 to December 2022 at the Liège University Hospital and Besançon University Hospital centers, for whom a diagnosis of esophageal motility disorders was confirmed by high-resolution manometry with an Eckardt score higher than 3 (>3). Patients who had already received a prior treatment for their motor disorder were not excluded. Patients younger than 18 years old were excluded from the study. On the basis of the patient's computerized medical record, an analysis was performed and had studied the pre-operative, operative and post-operative data.
Results: 89.1% of the patients had achalasia (mostly type II), and 10.9% had another esophageal motility disorder. The use of antibiotic prophylaxis was not systematic, only 44.4% of patients benefited from it. The mean value of the post-operative Eckardt score was 1.55 (± 2.48), with 93.2% of patients with a score of 3 or less. The rate of adverse event was generally low. The two most frequent adverse events in both centers were clinical capnomediastinum (12.7%) and bleeding during the procedure (10.9%). However, these adverse events could be managed intraoperatively, or did not require any particular management. Only 7.3% of the patients had an infectious phenomenon that did not correlate with the use of antibiotic prophylaxis.
Conclusions: In conclusion, the post-operative Eckardt score and the adverse event rate were comparable between the two university centers. This study confirms that POEM is a safe and effective endoscopic technique that can be rapidly acquired by an endoscopic expert. This study also shows that using an antibiotic prophylaxis does not influence the development of infectious adverse events.

- G16 -

A SURVEY AMONG FLEMISH GASTROENTEROLOGISTS ABOUT ENDOSCOPIC SEDATION PRACTICES IN COLORECTAL CANCER SCREENING. S. Arnaert (1), V. Vandebroek (1), D. Persyn (1), M. Cool (1), G. Lambrecht (1), G. Desmet (2), G. Deboever (1) / [1] AZ Damiaan, Oostende, Belgium, Gastroenterology, [2] AZ Damiaan, Oostende, Belgium, Pneumology.

Introduction: The sedation levels and methods used for colonoscopy in colorectal cancer screening programs vary from country to country and from continent to continent. Little is known in the literature about how frequently the different sedation levels are used in colorectal cancer screening colonoscopies.
Aim: We made a survey among all Flemish gastroenterologists (GI) to determine how frequently they use the different sedation modalities in this target population and to determine the motives of the GI to opt for one or another sedation modality.
Methods: An online survey was sent to all 329 Flemish GI by e-mail. A reminder e-mail was sent one month later. Participants could indicate how frequently (by percentage) they used the different sedation methods (no sedation, minimal sedation, conscious sedation, deep sedation) and which sedative medication they administered. In addition, they were asked to indicate their main motives for choosing a specific sedation method. Descriptive statistics were used.
Results: 112 out of 329 GI answered the questionnaire (response rate 34%). Anesthesia monitored care is the most frequently used sedation modality, followed by conscious sedation. Patient preference is the main motive for most GI to use each sedation modality.
Conclusions: Anesthesia monitored care is currently the most frequently used sedation regimen to perform a colonoscopy in the FIT positive population or in the colorectal cancer screening program in Flanders. The motives given by the GI for choosing one or another sedation modality are not always congruent with current scientific evidence or guidelines.

- G17 -

FIRST EXPERIENCES OF A NOVEL LARGE BORE RESECTION DEVICE (ENDOROTOR 6.0) USED IN THE ENDOSCOPIC TREATMENT OF WALLED-OFF PANCREATIC NECROSIS. M. Staessens (1), H. De Schepper (2), A. Jauregui Amezaga (2), M. Somers (2), S. Bouhadan (2), K. Krishnadath (2), S. Francque (2), E. Macken (2) / [1] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastro-enterologie en hepatologie, [2] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastro-enterologie en hepatologie.

Introduction: The primary management of infected and symptomatic walled-off pancreatic necrosis (WOPN) has gradually shifted from an invasive management with percutaneous drainage, laparoscopic or open necrosectomy to an endoscopic approach using the lumen apposing metal stent (LAMS) as an entry to the collection. However, one of the limitations of the endoscopic approach is the lack of effective and dedicated materials to remove the necrotic tissue.

The development of an endoscopic resection device (EndoRotor) has enabled a more controlled resection, although experiences and scientific data using this device in endoscopic necrosectomy are quite limited. We present our first impressions of the newest version of the EndoRotor (NecroMax 6.0) in a case series.
Aim: To assess the efficacy, practicality and safety of the EndoRotor device in the endoscopic treatment of WOPN.
Methods: In this retrospective case series, we reviewed data from four patients who underwent endoscopic necrosectomy (EN) between august 2023 and november 2023. All procedures were performed under general anesthesia, after prior placement of a LAMS (HotAxios 10 x 20 mm, Boston Scientific) at least 1 week prior to minimise the risk of stent migration. All necrosectomies were performed by two endoscopists (MS, EM) with no prior experience with the device. Device The EndoRotor 6.0 (NecroMax 6.0, Interscope Medical, Massachusetts, USA) is a large bore mechanical endoscopic resection system with a fixed outer cannula and a hollow inner cannula. A motorized, rotating cutting tool performs tissue resection at 1000 – 1700 revolutions per minute. As the catheter is connected to a vacuum suction channel, the resected tissue is immediately aspirated from the resection site as it is cut by the rotating inner cannula, and collected in the tissue collection trap. The cutting tool and the suction are controlled by the endoscopist using two separate foot pedals. It has an outer diameter of 6 mm, and can be used by an endoscope with 6 mm working channel (Olympus GIF-XTQ160 gastroscope, Olympus Corp., Japan) or using an adapter (EndoRotor catheter guide adapter) which is attached to the distal end of the endoscope, while the catheter is taped to the endoscope shaft. The catheter can be rotated 360° using an external handle to align the rotating blade to the necrosis. The channel of the catheter can be irrigated in an external fashion to avoid or resolve impaction of the necrosis.
Results: In total, 11 EN sessions with the EndoRotor device were performed in 4 patients with a median age of 57 years old [57, IQR 9,5]. Three out of four patients were male (75%). The etiology of the necrotising pancreatitis was heterogeneous and consisted of biliary pancreatitis (n = 2), post-ERCP pancreatitis (n = 1) and traumatic duct disruption with associated pancreatitis (n = 1). The median laterolateral diameter of the collection prior to the first EN was 115 mm [93 – 136, IQR 43]. The median procedure time was 78 minutes [50 – 108, IQR 58]. In three patients (75%), the collection had fully resolved on CT-scan two weeks after the last EN. The average amount of procedures needed to achieve a total necrosectomy was 1,25. In one patient, the collection had been reduced from 140 mm to 82 mm (reduction of 42%) after which EN was halted due to significant clinical improvement. Clinical improvement was achieved in all patients (100%). We performed 10 procedures using Olympus GIF-XTQ160 gastroscope with the catheter through the channel. In 1 procedure, we attached the EndoRotor to the end of a gastroscope (Fujifilm EG-720R) using the catheter adapter. During this procedure, the LAMS had migrated into the WOPN due to difficult access through the LAMS. However, since the procedure was completed using the existent trajectory with complete drainage of the necrosis, there was no need to replace the LAMS. In one necrosectomy (9,1%), a technical failure of the rotating blades ensued due to aspirated sutures from the WOPN. The procedure could be completed by replacing the catheter. No procedure-related adverse events occurred.
Conclusions: Our initial experience with the EndoRotor suggest that this device is effective and can be safely used for endoscopic necrosectomy of infected walled-off pancreatic necrosis. More data are needed to assess the efficacy, safety and cost-effectiveness of this treatment.

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THE PRESENCE OF SCARRING DOES NOT SIGNIFICANTLY IMPACT BLINK DECISION MAKING REGARDING CANCER IN LARGE NON-PEDUNCULATED COLORECTAL POLYPS BUT REPRODUCIBLY ALTERS THE PATTERN OF BLINK FEATURES IDENTIFIED AMONGST NON-EXPERT ENDOSCOPISTS.

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Introduction: Cancer in large non-pedunculated colorectal polyps (LNPCPs) is poorly discriminated outside expert centres. Identification of 6 blink features (6BF) of cancer has shown significant improvement in the sensitivity of submucosal invasive cancer (SMI) detection in LNPCPs by inexperienced endoscopists at the expense of decreased specificity. Endoscopic resection scars mimic the appearance of deep SMI [via intense submucosal fibrosis] upon which 6BF are based and may confound blink decision-making.
Aim: We aimed to investigate whether the presence of scars confounds the interpretation of 6BF by non-expert endoscopists.
Methods: An online survey was disseminated containing 20 overview images of LNPCPs (1 image/polyp) to a mailing list of >3000 endoscopists of varying experience. Images (randomized) were shown before, and again after a 2-minute educational video (the intervention) which introduced 6 macroscopic (Blink) features of deep SMI - fold deformation, extra redness, depression, chicken skin mucosa, ulceration and spontaneous bleeding. Prior to the intervention participant Blink impression was elicited (cancer/no cancer). After the intervention the same question was asked, and participants were required to describe which of 6BF were present. An experienced participant was defined as having performed ≥50EMRs and ≥1000 colonoscopies. The primary endpoint was the analysis of 6BF relative to histopathology (no versus

superficial [<1000µm] versus deep [>1000µm] SMI) and expert consensus on the presence of the 6BF and the presence of endoscopic resection scars.
Results: 7/20 LNPCPs shown, histologically contained cancer (3 superficial, 4 deep). 3 contained scars. 191 participants from 21 countries completed 3,755 observations. 129/191 (67.5%) participants were inexperienced. Expert-identified scarred LNPCPs contained median 1.0 (Interquartile Range [IQR] 2.0) BF versus 1.0 (IQR2.0) for no cancer, 2.0 (IQR2.0) for superficial cancer and 3.0 (IQR2.0) for deep SMI, all P<.001. Presence of ≥2BF therefore reliably identifies cancer within LNPCPs but does not identify scars. Fold deformation was the only BF identified more commonly amongst scarred LNPCPs (44.6%[95% confidence interval (95%CI) 40.6-48.7]) versus no cancer (22.5%[95%CI 20.6-24.4], P<.001) and versus superficial SMI (33.0%[95%CI 29.1-36.9], P<.001), but similar to deep SMI (44.6%[95%CI 41.2-48.2], P=1.000). Depression, chicken skin mucosa and spontaneous bleeding were less commonly identified in scarred polyps (12.3%[95%CI 9.6-15.0], 7.6%[95%CI 5.4-9.7] and 1.8% [95%CI 0.7-2.8]) than both no cancer (33.1%[95%CI 31.0-35.2], 14.4%[95%CI 12.8-16.0] and 8.6% [95%CI 7.6-10.1], all P<.001), superficial SMI (68.6% [95%CI 64.8-72.4], 14.3%[95%CI 11.4-17.2] and 5.8%[95%CI 3.9-7.8], all P<.001) or deeply invasive polyps (45.9% [95%CI 42.3-49.4], 19.6% [95%CI 16.8-22.4] and 40.5% [95%CI 37.0-44.0], all P<.001). Extra redness and ulceration were identified with similar frequency to no cancer in scars (26.4%[95%CI22.7-30.0] versus 26.8%[95%CI 24.8-28.8], P=0.891 and 10.2%[95%CI7.7-12.7] versus 9%[95%CI 7.7-10.3], P=0.441 respectively), but less commonly than superficial (64.2%[95%CI60.3-68.1], P<.001 and 15.7%[95%CI12.7-16.7], P<.001) or deep SMI (60.2%[95%CI56.7-63.7), P<.001 and 24.7%[95%CI 21.6-27.8], P<.001). The sensitivity and specificity of Blink impression (versus histopathology) after the intervention was 88.2%(95%CI 86.3-90.0) and 55.1%(95%CI 53.0-57.2) respectively for cancer when scars were included and 88.2%(95%CI 86.3-90.0) and 54.5%(95%CI 52.1-56.9) when excluded.
Conclusions: Scarred LNPCPs exhibit fold deformation at a similar rate to deep submucosally invasive LNPCPs at first impression. Other BF are similar (extra redness and ulceration) or less pronounced (depression, chicken skin mucosa and spontaneous bleeding). Importantly the presence of ≥2BF still reliably discriminates LNPCPs with cancer from no cancer in the presence of scarred polyps. These findings are important for the non-expert detection of cancer in LNPCPs.

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INTRAVENOUS LIDOCAINE: IMPACT ON COUGH DURING GASTROSCOPIES. O. Assam (1), C. Boudart (2), V. Huberty (3) / [1] Erasme Hospital, Brussels, Belgium, Anesthesiology, [2] Erasme Hospital, Brussels, Belgium, Anesthesiology, [3] Erasme Hospital, Brussels, Belgium, Gastroenterology.

Introduction: Gastroscopy can induce cough, nausea, throat discomfort, abdominal discomfort, perforation, and bleeding. Sedation is crucial to enhance patient comfort and examination quality (Zheng et al. ;2018). Propofol is the preferred anesthetic agent. However, it can lead to adverse effects if underdosed: cough, involuntary body movements, laryngospasm, bronchospasm, and, in cases of overdose, desaturation, hypotension, apnea, and cardiac arrest (Hinkelbein et al. ;2018, Stogiannou et al.;2018). Lidocaine might reduce propofol consumption and the side effects of both propofol and gastroscopy (Hu et al. ;2022, Liu et al. ;2020, Qui et al. ;2022).
Aim: The objective of this study was to assess propofol consumption when intravenous lidocaine was added during gastroscopy, as well as its impact on cough and the gastroenterologist's satisfaction.
Methods: 46 ASA 1-2 patients under the age of 65 were randomized to receive either 1.5 mg/kg of lidocaine (Lidocaine Group) or a placebo (Control Group). Sedation was achieved by administering propofol with a target-controlled infusion based on bispectral index. The primary endpoint was propofol consumption between the two groups. Secondary endpoints included the presence of cough, involuntary movements, hypoxemia, hypotension, tinnitus, metallic taste, and gastroenterologist satisfaction.
Results: Lidocaine did not reduce propofol consumption but did decrease the occurrence of cough during gastroscope insertion; 9% cough with lidocaine vs. 52% in the control group (p=0.002). The incidence of involuntary movements, hypotension, desaturation, and gastroenterologist satisfaction were comparable. Only patients who received lidocaine experienced tinnitus (52% ; p<0.001) and a metallic taste (28% ; p=0.004).
Conclusions: Intravenous lidocaine reduces significantly cough during gastroscope. Lidocaine administration was associated with a significant rate of minor side effects from local anesthetics.

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EMERGENCY ERCP DURING THE WEEKEND: INDICATIONS, PROCEDURES AND OUTCOMES. B. Weicker (1), L. Monino (1), P. Deprez (1), H. Piessevaux (1), T. Moreels (2) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Hépato-Gastro-Entérologie, [2] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Hépato-Gastro-Entérologie.
Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is a complex procedure combining both endoscopy and fluoroscopy to treat pathology of the biliopancreatic system. Outcomes may vary with the endoscopists' experience and the procedure is prone to life-threatening adverse events. Little information is known about the outcome of emergency ERCP performed during the weekend or on holidays.

Aim: Retrospective analysis of emergency ERCP during the weekend between 2019-2023.
Methods: All patients who underwent emergency ERCP during the weekend or a holiday were included in the database. Analysis started from 2019 onwards. Patient and procedure characteristics were registered: ERCP indication, procedure and outcome, time between hospitalisation and emergency ERPC, length of stay and in-hospital mortality.
Results: From 2019 onwards, 31 emergency ERCP procedures were scheduled during the weekend in 30 patients with a mean age of 60±4 years (range 2-92) and an equal male/female ratio. This represents 0.3-1.3% of total annual ERCP number. All procedures were considered urgent based on clinical presentation (fever 39%, sepsis 36% with shock 23%) or on radiological findings. In 24 ERCP procedures indications were (suspicion of) obstructive common bile duct stone (71%), postoperative biliary leak (13%), malignant biliary obstruction with cholangitis (13%), traumatic pancreatic rupture (4%). In the 7 remaining procedures, indications required an alternative technique: endoscopic ultrasound (EUS)-guided drainage of the gallbladder or a pancreatic pseudocyst (10%), treatment of post-sphincterotomy bleeding (10%) and treatment of a gastric perforation after EUS-guided drainage (3%). Procedures were performed within 12h after admittance (29%), within 24h (58%), 48h (10%) or 72h (3%) either in a dedicated ERCP room (90%), in the operation room (7%) or in the intensive care unit (3%). All 24 conventional ERCP procedures were technically successful, with sphincterotomy and stone extraction in 50% of the patients, stent placement in 7 patients (29%, 4 plastic stents and 3 metal stents) and 1 balloon dilatation of a biliary stricture (4%). Although post-ERCP pancreatitis and cholangitis were not present in this patient cohort, 5 ERCP procedures were complicated by per- or post-procedural biliary or sphincterotomy bleeding (21%) requiring intervention by means of local balloon compression, fully-covered metal stent placement, submucosal epinephrine injection, bipolar coagulation and blood transfusion. Bleeding was not related to the concomitant use of antiaggregant or anticoagulant medication. Mean total hospital stay was 22±6 days (range 2-100) and one patient died within 15 days after the ERCP procedure due to progression of the underlying hematological malignancy. There was no ERCP-related mortality.
Conclusions: Emergency ERCP during the weekend represent a small fraction of total annual ERCP numbers, leading to prolonged hospital stay. The vast majority of indications encompasses (septic) cholangitis due to biliary stones. Technical success is high with a good safety profile, even when performed in other rooms than the dedicated ERCP room. However, the risk of per- and post-procedural bleeding (biliary or post-sphincterotomy) is higher (21%) than expected, irrespective of the concomitant use of antiaggregant/anticoagulant medication.

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RISK FACTORS FOR POST-ERCP INFECTION AND INDICATIONS FOR SINGLE-USE DUODENOSCOPES IN A LARGE COHORT OF PATIENTS IN ACADEMIC AND NON-ACADEMIC CENTERS. M. Lucion (1), V. Putzeys (2), H. Piessevaux (1), P. Deprez (3) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Hepatogastroenterology, [2] CHR Citadelle, Liège, Belgium, Hepatogastroenterology, [3] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Gastro-entérologie.

Introduction: Evidence of MDRO epidemics due to the use of reusable duodenoscopes led to the design of the single-use duodenoscope (SUD), in the hope that its use would prevent such infections. Having proven the technical efficacy and safety of the SUD, several consensuses have attempted to discern the indications for its use. These indications remain broad, despite the economic and ecological cost of these devices.
Aim: The aim of our study was to determine the risk factors for post-ERCP infection and indications for SUD use, in a large cohort of patients undergoing ERCP in an academic and a non-academic center.
Methods: We conducted a longitudinal, retrospective study including all ERCPs performed in an academic center and in a non-academic center between July 1, 2021 and June 30, 2022, based on a prospective registry. Age, gender, indications for ERCP, potential risk factors for post-ERCP infections and indications for SUD use, previous procedure, presence of active pre-ERCP infection and/or MDRO carriage, use of antibiotic therapy prior to ERCP, and technical procedures performed during ERCP were recorded at inclusion. The primary outcome was the incidence of infection occurring within 30 days of ERCP. Post-ERCP infection was defined as any evidence of a new infection after the ERCP procedure, in the absence of a more likely infectious etiology other than ERCP, and in the absence of a pre-ERCP infection. Post-ERCP cholangitis and cholecystitis were defined in accordance with the Tokyo 2018 guidelines. Type of infection (either cholangitis, cholecystitis, liver abcess, peritonitis, pneumonia, urinary tract infection, septicemia, pseudocyst or WON infection, and other), AGREE classification for the AE that occurred, length of stay pre- and post-ERCP, intensive care unit (ICU) admission, germ type, duration of antibiotic therapy and type of antibiotic therapy were also recorded.
Results: In these 654 ERCPs (including 539 and 115 procedures performed in an academic and non academic center, respectively), the mean age was 61 y (60± 18). Infection was the more prevalent AE accounting for 54 patients (8.2%). Of these patients, 42 (77,8%) had one or more risk factors. In univariate analysis, ERCP outcome (complete or incomplete drainage) ($p<0,0005$), the presence of hilar/Klatskin tumor ($p=0.001$ and $p=0.004$, respectively), Spyscope use ($p=0,010$), presence of liver metastasis ($p=0,014$), post-surgical stenosis ($p=0,035$), plastic biliary stenting ($p=0,046$), and ongoing chemotherapy and hematologic disease ($p=0,047$) were associated with post-ERCP infection. In multivariate analysis, the presence of a Klatskin tumor ($p<0.0005$), hematological disease ($p=0,021$), ongoing chemotherapy ($p=0,001$), benign biliary stricture ($p=0,027$), were significantly associated with post-ERCP infection, for a total of 236 patients. Moreover,

including HIV+ (1pt), Covid+ (4pts) and MDRO-infected or -carriers patients (14pts), 247 pts were potential indications for SUD use.
Conclusions: Multivariate analysis showed that the presence of a Klatskin tumor, hematological disease, ongoing chemotherapy, and benign biliary strictures were significantly associated with post-ERCP infection. Taking into account HIV-, Covid- and MDRO infected or carriers- patients, the total theoretical indications for SUD includes 37,8% of all ERCPs. Further research is needed to determine the cost-benefit of SUD use and whether or not these infections may be scope related.

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ENDOSCOPIC SUBMUCOSAL DISSECTION USING GEL SOLUTION VERSUS GLYCEROL FOR SUBMUCOSAL INJECTION: A RANDOMIZED CONTROLLED MULTI-CENTRIC TRIAL. G. Losurdo (1), A. Bucalau (1), P. Eisendrath (1), V. Huberty (1), H. Neuhaus (2), T. Veiser (2), N. Yahagi (3), J. Peetermans (4), M. Rousseau (4), T. Beyna (2), A. Lemmers (1) / [1] Erasme Hospital, Brussels, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, [2] Evangelisches Krankenhaus Düsseldorf, Dusselforf, Germany, Department of Internal Medicine, [3] Keio University School of Medicine, Tokyo, Japan, Division of Research and Development for Minimally Invasive Treatment, [4] Boston Scientific Corporation, Marlborough, United States, Boston Scientific.

Introduction: Submucosal injection is a crucial step when performing endoscopic submucosal dissection (ESD). Glycerol is the most used solution that has been implemented, however novel formulations are emerging.
Aim: This study aimed to comparatively evaluate the submucosal injection using a gel solution versus glycerol during ESD procedures in patients with superficial gastric and rectal (pre)malignant lesions.
Methods: We conducted a prospective multicenter randomized controlled trial in patients with documented gastric or rectal lesions indicated for ESD. Primary endpoint was dissection speed, defined as the dissected surface (mm2)/ESD duration (min). The enrollment goal was 266 patients randomized in 1:1 ratio assuming the gel solution would increase the dissection speed by 5.13 mm2/min or ~23% compared to glycerol, based in historic data at the coordinating center. Other endpoints included rate of en bloc resection, complete endoscopic resection, total hemostatic time, need for hemostatic forceps during procedure and serious adverse events, evaluated by AGREE classification. ClinicalTrial NCT04977401.
Results: We randomized 31 patients (mean age 67, 58% male), 16 to gel group and 15 to glycerol group at 2 centers. The trial was discontinued early because the gel solution was withdrawn from market by the manufacturer. Nine lesions in the stomach and 22 in the rectum were resected. The mean dissection speed in the gel group was 34.4±14.6 vs 25.7±14.0 mm2/min in the glycerol group, which is 25% faster, but the a priori test did not reach statistical significance due to small sample size (p=0.100). Dissection speed was higher in gastric lesions for gel solution than for glycerol (33.1±11.7 vs 17.9±8.4 mm2/min, p=0.065). En bloc resection was similar between the groups with each group having one lesion not dissected en bloc. Complete endoscopic resection was achieved in all lesions that had en bloc resection. The mean number of intraprocedural bleeds per procedure was similar, but we observed less need of hemostatic forceps for bleeding control in the gel group (56% vs 87%, p=0.113). Total hemostatic time was 18.6±31.3 and 23.0±30.1 minutes for gel and glycerol respectively. There were 4 major adverse events (grade IIIa), 3 serious bleeds in the gel group and 1 perforation in the glycerol group (p=0.600). Two bleeds occurred after procedure, day 7 and 10, requiring blood transfusion and all 3 episodes were treated endoscopically. The perforation was treated endoscopically with 3 clips.
Conclusions: Although this trial was stopped early, this small, randomized trial showed a potential increase of ESD dissection speed with gel solutions over glycerol, with similar resection success and a trend towards a lower need for hemostatic forceps. Further research into different types of lifting agents is warranted.

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PARIS-IS NODULES ≥10MM COMMONLY OCCUR IN LARGE GRANULAR LESIONS AND ARE A RISK FACTOR FOR SUPERFICIAL SUBMUCOSAL INVASIVE CANCER. P. Poortmans (1), L. Debels (1), S. Smeets (2), M. Argenziano (2), M. Montori (2), S. Ridolfo (2), T. Tornai (2), L. Desomer (3), N. Burgess (4), M. Bourke (4), D. Tate (2) / [1] UZ Brussel, Brussels, Belgium, Gastroenterology and Hepatology, [2] Universitair ziekenhuis Gent, Belgium, Gastroenterology and Hepatology, [3] AZ Delta, Roeselare, Belgium, Gastroenterology and Hepatology, [4] Westmead Hospital, Sydney, Australia, Gastroenterology and Hepatology.

Introduction: Colorectal cancer leads to poor patient outcomes. Cancer in large colonic laterally spreading lesions (LSLs) may be unrecognised if it is not visible on the surface (COVERT cancer). COVERT disease is predominantly located in the rectum and has shown to be poorly recognised by endoscopists. It is unknown whether the size of the dominant nodule (Is component) in LSLs with nodular/Is component is correlated with risk of cancer or depth of submucosal invasion (SMI).
Aim: To investigate the relationship between Is component size and number with risk and depth of SMI.
Methods: We analysed endoscopic appearance and histopathology of LSLs ≥ 20 mm from a prospectively collected multicenter database of polyps referred for endoscopic resection between November 2017 and November 2023. Visible

(OVERT) cancers were removed. We compared all LSLs without large Is component (≥10mm) to all LSLs with large Is component (Paris 0-Is and 0-IIa+Is polyps with Is component ≥10mm). The primary end point was correlation of large nodular component in LSLs with SMI. Secondary end points were correlation of large nodular component in LSLs with other risk factors for COVERT disease (location in the colon, size and morphology).
Results: A total of 265 LSLs with and 3205 LSLs without large Is component were included in the analysis. A large Is component was found more often in LSLs ≥40mm in size (56.98% [95% confidence interval (95% CI) 51.02% - 62.94%] vs. 37.78% [95% CI 36.11% - 39.46%], P<0.01), in granular polyps (86.79% [95% CI 82.72% - 90.87%] vs. 58.0% [95% CI 56.29% - 59.71%], P<0.01) and in the rectum (33.96% [95% CI 28.26% - 39.66%] vs. 16.41% [95% CI15.13% - 17.69%], P<0.01) when compared to LSLs without large Is component. LSLs with large Is component were more likely to contain SMI than LSLs without large Is component (4.91% [95% CI 2.31% - 7.51%] vs. 2.09% [95% CI 1.60% - 2.59%], P<0.01). When stratifying for depth of SMI, LSLs with a large nodular component were more likely to contain superficially invasive cancer (2.26% [95% CI 0.47% - 4.06%] vs. 0.72% [95% CI 0.43% - 1.01%], P=0.01) but not deeply invasive cancer (2.64% [95% CI 0.71% - 4.57%] vs. 1.37% [95% CI 0.97% - 1.78%], P=0.17) when compared to LSLs without large Is component.
Conclusions: Large colonic laterally spreading lesions with a ≥10mm Is component are more likely to be situated in the rectum, be ≥40mm in maximum dimension and granular in morphology. A dominant nodule of ≥10mm increases the risk of cancer within LSLs. These lesions are more likely to contain superficial SMI than lesions without a large Is component, but not deep SMI. These results have implications for the prediction of COVERT disease, choice of resection technique and stratification of patients to standard of care treatment first time.

- G24 -

CRIS: A NOVEL TOOL DESCRIBED USING ONLY THREE SELF-EXPLANATORY WORDS PERFORMS SIMILARLY TO JNET AMONGST WESTERN EXPERTS IN THE DETECTION OF CANCER AND DETERMINATION OF CORRECT TREATMENT IN LARGE NON-PEDUNCULATED COLORECTAL POLYPS. M. Argenziano (1), L. Debels (2), S. Smeets (2), M. Montori (2), P. Poortmans (3), S. Ridolfo (2), T. Tornai (2), M. Kaminski (4), V. Lala (5), R. Valori (6), J. Anderson (6), M. Bourke (7), L. Desomer (8), D. Tate (2) / [1] University Hospital of Ghent, Belgium, Gastrointestinal and Liver Diseases, [2] University Hospital of Ghent, Belgium, Gastrointestinal and Liver Diseases, [3] University Hospital Brussels, Vrije Universiteit Brussel, Belgium, Gastroenterology, [4] Maria Sklodowska-Curie Memorial Cancer Centre, Warsaw, Poland, Gastroenterological Oncology, [5] Charlotte Maxeke Johannesburg Academic Hospital, Johannesburg, South Africa, Gastroenterology, [6] Cheltenham General Hospital, Cheltenham, United Kingdom, Gastroenterology, [7] Westmead Hospital, Sydney, Australia, Gastroenterology, [8] AZ Delta, Roeselare, Belgium, Gastroenterology.

Introduction: The JNET (Japan NBI Expert Team) classification can be used to predict large non-pedunculated colorectal polyp (LNPCP) histology and presence/depth of submucosal invasion (SMI). However, Japanese endoscopist accuracies >84% have not been replicated even amongst Western experts; for example, in a recent study of European experts the accuracy of JNET was 55%. Furthermore, European guidelines suggest both low-grade dysplasia (LGD) and high-grade dysplasia (HGD) can be treated using endoscopic mucosal resection (EMR) thus there is no clinical consequence to interpreting HGD as JNET 2A (excluded in the original interpretation of JNET).
Aim: We aimed to compare JNET with CRIS (Colorectal Regular-Irregular Score) for LNPCP histology prediction amongst Western experts using both the original JNET interpretation and the above-described clinically relevant approach.
Methods: 32 images of flat LNPCPs under narrow-band imaging were consecutively obtained with matched histopathology data. Each image was rated (anonymous online survey) using JNET and then all the images were rated again (order randomised) using CRIS, a novel score which simply asks whether the most disordered vascular pattern visible in the image is 'regular(=CRIS-R), regularly-irregular(=CRIS-RI) or completely-irregular(=CRIS-I)'. No further explanation of JNET or CRIS was offered. Accuracy of JNET and CRIS vs. histopathology was analysed using the original JNET interpretation (where JNET 1/2A and CRIS-R = LGD) and a clinically relevant approach (where JNET1/2A and CRIS-R can also = HGD). JNET2B & CRIS-RI were matched to HGD & superficial SMI and JNET3 & CRIS-I to deep SMI. Correct treatment was defined as pEMR for LGD or HGD, en-bloc EMR/ESD for HGD or superficial SMI and surgery for deep SMI.
Results: 12 experts (median 150 colorectal EMRs and 13 ESDs/year) rated 32 images. 8 low-quality images were excluded from the analysis. The overall accuracy of JNET vs. histopathology using the original interpretation was 69.7% (95%CI 46.0-89.3%) and CRIS 69.6% (95%CI 45.3-88.7%). Expert agreement was similar between JNET (91.3% [95% confidence interval (95%CI) 82.8-98.3%] and CRIS (88.5% [95%CI 78.2-97.3%]) with K=0.64 (substantial) for JNET and K=0.57 (moderate) for CRIS. Specifically, the accuracy of JNET 2b was found to be 51.7% (95% CI 45.9-57.4%), in comparison, JNET 3 demonstrated a higher accuracy of 85.8% (81.2-89.3%). A comparable result was observed for CRIS-RI and CRIS-I, which showed accuracies of 51% (45.2-56.7%) and 85.1% (80.4 - 88.7%), respectively. Correct treatment was determined in 144/288 (50.0%) observations using JNET and 144 (50.0%) using CRIS. The overall accuracy of JNET vs. histopathology using the clinically relevant approach was 73.9% (95%CI 46.0-89.3%) vs. CRIS 72.3% (95%CI 45.3-88.7%). The accuracy, sensitivity and specificity of JNET 1/2A changed by 13.2%, -8.0% and 38.0%

and CRIS-R by 8.3%, -8.2% and 35.5%. Correct treatment determination increased by 29.5% to 79.5% for JNET and by 27.1% to 77.1% for CRIS.
Conclusions: High rates of accuracy can be obtained by Western experts using JNET to predict histology of colorectal LNPCPs. Similar accuracy is obtained using CRIS, a novel score named and described by 3 self-explanatory words suggesting JNET may be able to be simplified for non-experts. Importantly the specificity of both systems can be increased by framing their interpretation versus. histology in a clinically relevant fashion. This has significant implications for signposting patients to correct treatment after detection of LNPCPs especially amongst non-experts.

- G25 -

LAMS OBSTRUCTION LITHOTRIPSY (LOL) - ELECTROHYDRAULIC LITHOTRIPSY OF A GALLSTONE IMPACTED IN A LUMEN APPOSING METAL STENT POSITIONED FOR CHOLECYSTO-DUODENOSTOMY.
V. VandenDriessche (1), P. Yengue (1), M. Lefebvre (1) / [1] Centre Hospitalier Wallonie Picarde (CHWAPI), Tournai, Belgium, Gastro-entérologie.

Introduction: Previous research has emphasised the growing significance of employing endoscopic ultrasound (EUS)-guided gallbladder drainage using Lumen Apposing Metal Stents (LAMS) for cases of acute cholecystitis. This is particularly relevant when conventional approaches such as endoscopic retrograde cholangio-pancreatography (ERCP) or surgical procedures are not feasible. Comparative analyses have indicated a lower incidence of adverse events associated with EUS-guided gallbladder drainage by LAMS, as opposed to percutaneous intervention. Nonetheless, these adverse events encompass potential complications such as gastrointestinal bleeding, stent migration and, in rare occurrences, obstruction of the LAMS by a large bile stone. Removing biliary LAMS obstructions typically requires mechanical lithotripsy (ML) or electrohydraulic lithotripsy (EHL). However, to our knowledge, only two other instances have been documented resolving LAMS obstruction using EHL. One of these cases highlights the effective utilisation of EHL in eliminating a cholecystogastrostomy obstruction, while the other presents a scenario where a combination of mechanical lithotripsy and EHL was employed to resolve a cholecystoduodenostomy blockage.
Aim: To demonstrate the feasibility of EHL as a standalone approach for managing cholecystoduodenostomy bile stone obstructions.
Methods: In this case study, we present an 84-year-old patient afflicted by acute cholecystitis who was not eligible for surgery due to her advanced age and comorbidities (urothelial carcinoma, hypertension, and polymyalgia rheumatica). Initial treatment consisted of percutaneous drainage and antibiotic treatment, resulting in a prompt clinical resolution. However, three months later, the patient experienced recurrent cholecystitis. Surgical cholecystectomy was considered but deemed too invasive for this frail elderly patient. As a result, we opted for EUS-guided gallbladder drainage, creating a cholecysto-bulbostomy and inserting a 15 mm diameter Lumen Apposing Metal Stent (LAMS). Unfortunately, the procedure was complicated by pneumoperitoneum, which we promptly addressed with needle exsufflation. Fortunately, the patient exhibited a positive clinical response while hospitalised and was consequently discharged. Four months later, upper right abdominal discomfort arose, accompanied by sepsis. Endoscopic ultrasound-guided fluoroscopy revealed a 20 mm bile stone obstructing the cholecystoduodenostomy by LAMS, which led to early gangrenous cholecystitis. This prompted the endoscopic management by SpyGlass-guided electrohydraulic lithotripsy (SGEHL) of the macrolithiasis with the removal of stone debris by endoscopic loop. Subsequently, a double-pigtail plastic biliary stent was placed through the LAMS to ensure correct LAMS stability.
Results: The control abdominal CT scan showed a significant reduction in the previously observed gallbladder wall oedema and no signs of complications. The bile culture returned positive for E. coli, Klebsiella pneumoniae, and Candida albicans. Blood results showed a critical increase in C- reactive protein levels, white blood cell count, and neutrophil levels. Empirical antibiotic therapy was subsequently initiated with ciprofloxacin and metronidazole, followed by a switch to cefepime after the antibiogram realisation for ten days of antibiotic coverage. Inflammatory markers progressively decreased, and the patient was discharged.
Conclusions: We hereby demonstrate the successful management of cholecystoduodenal LAMS obstruction using a standalone EHL approach or LOL. While two previous case reports have shown success in treating biliary LAMS obstruction by EHL, our case study confirms the effectiveness of EHL without mechanical lithotripsy in a cholecysto-duodenal LAMS. EUS-guided gallbladder drainage is rapidly gaining widespread use, which inevitably leads to an increase in the incidence of LAMS-associated adverse events. LAMS obstruction, in particular, poses a significant sepsis risk, prompting the need for new treatment strategies to address previously inexisting complications. The main concern with electrohydraulic lithotripsy is the risk of perforation, which can occur when the EHL probe either makes direct contact with the wall or significantly increases the temperature of the stone surface and surrounding tissue. In a series of cases involving the use of EHL to address bile duct and pancreatic duct stones, this risk of perforation was estimated to be less than 1%. The main advantage of LOL is that it allows for a minimally invasive approach compared to surgical intervention in a population of fragile patients, where gallbladder drainage was initially treated endoscopically as opposed to invasive surgery. Thus, LOL could be a valuable addition to our current therapeutic arsenal for managing inoperable patients presenting biliary LAMS obstruction. Further research in larger patient cohorts is necessary to assess LOL's safety and efficacy profiles to treat biliary LAMS obstruction.

- G26 -

ENDOSCOPIC AMPULLECTOMY ASSOCIATED WITH INTRADUCTAL RADIOFREQUENCY: A NEW APPROACH FOR THE TREATMENT OF AMPULLOMAS. C. Vasconcelos (1), A. El Nawar (2), P. Yengue (2), M. Lefebvre (2) / [1] Centre Hospitalier de Wallonie Picarde (CHWAPI), Tournai, Belgium, Gastroenterology, [2] Centre Hospitalier Wallonie Picarde (CHWAPI), Tournai, Belgium, Hepatogastroenterology.

Introduction: Ampullary tumors represent less than 1% of all digestive tumors. Because of the histological transition that characterizes the ampulla of Vater region two histological subsets exist: the intestinal subset developing from duodenal adenomas and the pancreatobiliary subset developing from the pancreatobiliary duct epithelium. Ampullomas can degenerate to carcinoma passing through stages of low- and high-grade dysplasia (1). Multiple endoscopic aspects can be found. A diagnosis can be easily made when the lesion is a vegetive extra-ampullary mass, intra-ampullary lesions are more difficult to detect but mixed intra and extra-ampullary tumors are the most frequent. Staging has been made easy thanks to the development of endoscopic ultrasound that allows us to determine the depth of invasion, intraductal invasion and lymph node involvement. Treating these lesions remains a challenge because of the lack of guidelines that push us to be creative. The development of endoscopic techniques of resection has made it possible to decrease the morbidity and mortality associated with pancreatoduodenectomy. Intraductal invasion is usually limits the use of endoscopic resection but recent development of intraductal radiofrequency could change the way we treat these lesions.
Aim: In this paper we aim to demonstrate the use of endoscopic resection combined with intraductal radiofrequency in a case of extrapapillary ampulloma with invasion of the common biliary tract.
Methods: The study involves a 61-year-old patient diagnosed with a 2cm vegetive extraampullary mass during an endoscopic retrograde cholangiopancreatography performed for choledocholithiasis. Biopsies showed a papillary adenoma presenting low grade dysplasia and endoscopic ultrasound showed no muscularis invasion and no lymph node involvement but demonstrated intraductal invasion (TNM staging: T1). We performed an en bloc endoscopic papillectomy associated with sphincterotomy and resection of the intraductal invasion. The patient received biliary and prophylactic pancreatic duct stenting. Follow-up at 1, 3 and 8 months showed recurrence of the intraductal invasion needing multiple sessions of resection and coagulation of the remaining adenomatous glands. At this point, a visual analysis of the ductal extension was performed using a single-use cholangioscope (Spyglass, Boston) and surgical treatment (surgical papillectomy vs. Whipple) was proposed to the patient but refused due to morbidity/mortality and confirmation of only low-grade dysplasia in the resected lesion. After multi-disciplinary concertation we decided to use intraductal biliary radiofrequency ablation (RFA) to treat the recurrent intraductal growth. We used a Habib EndoHBP radiofrequency ductal probe (Boston), 8Fr bipolar catheter with two ring electrodes that induces necrosis over 2.5 cm, at the lower third of the biliary duct. Energy delivered in SoftCoag effect 8.8 Watt for 90 seconds, repeated 3x to cover the entire papillary circumference.
Results: We performed en bloc endoscopic papillectomy associated with one session of intraductal radiofrequency ablation for a 2cm papillary adenoma with intraductal invasion of the common bile duct. Follow-up at 3 and 6 months after complementary RFA showed no recurrence. The only complication was a significant biliary stenosis and pancreatic duct stenosis that manifested as acute pancreatitis and cholestasis treated by stenting.
Conclusions: Patients with ampullary adenomas with intraductal involvement are usually referred for surgical therapy because the high rate of recurrence associated with an endoscopic treatment (2). Emerging endoscopic techniques of resection and destruction could allow a significant decrease in the use surgical resection and therefore decrease the morbidity and mortality associated with surgical therapies. Tringali A and al studied 31 patients that underwent papillectomy for ampulloma. Eight of them had intraductal invasion of common bile duct (CBD) and one had CBD and pancreatic duct invasion treated by RFA. RFA settings were the same for all patients (10W for 120 sec.; ablation temperature 80°) and one to four sessions were needed. Clinical success at a median follow-up of 21 months was achieved by six patients (66.7%). Only one patient developed acute pancreatitis after pancreatic stenting failed during the second session of RFA and recovered fully (3). Sung Hyun Cho and al, described 29 patients (14 CBD, 1 PD, and 14 CBD and PD) that undergone endoscopic papillectomy associated with intraductal RFA. A median of one session of ID-RFA (range, 1 to 3) for intraductal extension of ampullary adenoma were successfully performed. Both biliary and pancreatic stenting were routinely performed after ID-RFA to prevent stenosis. The median follow-up was 776 days. Short-term and long-term clinical success rates were 93% and 76%, respectively (5). With this case we aim to demonstrate that the use of intraductal radiofrequency can be efficiently and safely used to treat residual adenomatous tissue extending from the papilla into the common bile duct. Other studies have shown the same tendency (3, 5) but more evidence and standardization is needed.

- G27 -

ENDOSCOPIC ULTRASOUND-GUIDED CYSTOGASTROSTOMY WITH LUMEN APPOSING METAL STENT FOR MANAGEMENT OF A HEPATIC ABSCESS. E. Kaya (1), V. VandenDriessche (1), P. Yengue (1), M. Lefebvre (1) / [1] Centre Hospitalier Wallonie Picarde (CHWAPI), Tournai, Belgium, Gastro-entérologie.

Introduction: Liver abscesses are defined as pus-filled masses in the liver that can originate from liver injury or abdominal infections disseminated by the portal vein circulation . The current standard of care for managing hepatic abscesses involves a combination of empiric antibiotic therapy, and percutaneous catheter drainage. In certain complex cases, surgical drainage is the preferred option, but its utilisation is decreasing due to its invasive nature. However, not all patients are suitable candidates for percutaneous drainage or for surgery. Therefore, there is a pressing need for less invasive endoscopic approaches, such as an EUS-guided LAMS placement for hepatic abscess drainage or ENDO-HEAL (ENdoscopic Drainage Of HEpatic Abscesses using LAMS).
Aim: To compare feasibility and safety of endoscopic ultrasound (EUS)-guided cystogastrostomy using a lumen apposing metal stent (LAMS) to ensure proper liver abscess drainage.
Methods: We present an 84-year-old woman hospitalised for acute abdominal pain, weight loss, and asthenia. Initial blood tests revealed elevated inflammatory markers, with C-reactive protein at 226 mg/L (normal range < 5 mg/L) and a neutrophil count of 9455 /µL (normal range 1800-7400 /µL). Liver enzymes were significantly altered: aspartate aminotransferase (AST) levels at 306 U/L (normal range 15-37 U/L), alanine aminotransferase (ALT) levels at 226 U/L (normal range 13-56 U/L), and lactate dehydrogenase (LDH) levels at 317 U/L (normal range 84-246 U/L). Cholestasis was evident with direct bilirubin at 0.75 mg/dL (normal range < 0.3 mg/dL). Gamma-glutamyl transferase (GGT) levels increased tenfold to 527 U/L (normal range 5-55 U/L), and alkaline phosphatase (ALP) levels rose fourfold to 481 U/L (normal range 35-104 U/L). Subsequent abdominal CT imaging revealed a 153 x 120 mm intracapsular liver abscess in her left hepatic lobe, leading to intrahepatic bile duct dilation. This abscess triggered sepsis and septic shock, with blood cultures identifying Streptococcus infantarius. Antibiotic treatment with cefuroxime and metronidazole was promptly initiated. At this point, percutaneous catheter drainage and surgical intervention were considered. However, due to the patient's advanced age and her pre-existing health conditions (including atrial fibrillation treated with direct oral anticoagulants, arterial hypertension, and obesity), she was deemed an unsuitable candidate after a multidisciplinary medical-surgical consult. An alternative, less invasive approach was chosen: EUS-guided cystogastrostomy for abscess drainage. A 15x10 mm LAMS was placed between the hepatic abscess and gastric cavity, with a subsequent plastic double pigtail stent for stability. Bacteriological analysis of the fluid extracted from the hepatic abscess confirmed the presence of Streptococcus infantarius, providing definitive confirmation of the sepsis's aetiology.
Results: We achieved complete resolution of the patient's symptoms, normalisation of inflammatory markers, and hepatic enzyme levels. An 80% decrease in abscess volume was observed on follow-up computed tomography imaging. Three months post-LAMS placement, a gastroscopy confirmed hepatic abscess resolution, allowing for the removal of both the LAMS and double-pigtail stent. No adverse events were observed.
Conclusions: In conclusion, this case report confirms the feasibility and safety of LAMS for draining hepatic abscesses and underscores the lifesaving potential in elderly and inoperable patients.

- G28 -

ENDOSCOPIC SUBMUCOSAL DISSECTION COMBINED WITH FULL THICKNESS RESECTION DEVICE: REPORT OF A CASE AND REVIEW OF THE LITERATURE. C. Vasconcelos (1), P. Yengue (2), J. Zeevaert (2), M. Lefebvre (2) / [1] Centre Hospitalier de Wallonie Picarde (CHWAPI), Tournai, Belgium, Gastro-Entérologie [2] Centre Hospitalier Wallonie Picarde (CHWAPI), Tournai, Belgium, Hépato-gastro-entérologie.

Introduction: Gastrointestinal polyps are commonly found in screening colonoscopy, as prevalence increases with age. A wide range of endoscopic procedures are available to provide en bloc resection. As Polypectomy is mostly used to treat superficial lesions, EMR (Endoscopy Mucosal Resection) and ESD (Endoscopy Submucosal Dissection) are performed to treat wider and deeper lesions [1]. ESD if used by an experienced physician is an effective widely and safely used technique not limited by the size or shape of the adenoma. Rare complications are associated with ESD such as perforation of the gastro-intestinal track, peritonitis, and hemorrhage. Risk factors for complications are unsuspected submucosal fibrosis, adenomas situated in the colon as the walls are thinner and non-liftable lesion associated with submucosal fibrosis [2,3,4]. FTRD is currently indicated for the treatment of recurrent adenomatous lesions previously treated by endoscopic resection, deeper lesions with submucosal invasion or fibrosis and difficult to access lesions. Even though this procedure provides a full wall thickness resection and therefore is not limited by the depth of invasion it is limited by the size of the cap, as adenomas larger than 40mm can't be incorporated in the cap [4].
Aim: The aim of this case report is to demonstrate that the use of a hybrid technique using ESD followed by Full Thickness Resection could be a way of treating lesions with unsuspected submucosal fibrosis.
Methods: This case report involves a 87 years old patient admitted for follow-up colonoscopy. She had a history of sigmoid adenocarcinoma (T3N0) treated by left colectomy in 11/2019 and a rectal polyp resected by endoscopy in 7/2021 histologically classified as an intramucosal adenocarcinoma. Full tract colonoscopy showed a polyp at 30 centimeters of the anal margin. The lesion was described as a LST-GT (laterally spreading tumor granular type), CONECCT IIc of 25mm. Patient was referred for ESD (Endoscopic submucosal dissection). ESD was performed with circumferential incision and dissection, using the rubber band and clips strategy plus submucosal injection of Glycéol 20%, adrenaline and indigo carmine. Unfortunately, the piece ripped apart within healthy margin and highlighted a thickened fibrotic area. As fibrosis limited further submucosal injection and lifting of the adenoma, ESD was interrupted and FTRD (Full

Thickness Resection Device) was performed to ensure R0 resection. The piece was trapped into the cap and resected en bloc clamp of 25x25mm.
Results: We performed ESD associated with FTRD to achieve R0 resection for a LST-GT Conecct IIc polyp of 25mm. Histology showed signet ring cells and classified the lesion as mucinous . invasive adenocarcinoma with healthy margin situated at 1cm. The scar showed no sign of complication. Antibiotic therapy was started for 3 days combined with a no waste diet and laxative to prevent infection of the wound. Patient was discharged 24h later. Follow-up at 1 year showed no recurrence.
Conclusions: Pretreatment biopsy limits the use of EMR or ESD as it's been shown to favor submucosal fibrosis and lead to complications and incomplete resection. In our case, no biopsies were performed when the adenoma was discovered and lifting sign was positive during injection. Even though observing the macroscopic aspects or the pit pattern of the adenoma can help predict the degree of submucosal fibrosis, unsuspected submucosal fibrosis has been shown to be a major risk factor of perforation during EMR or ESD. Andrisani G and al described 5 cases of hybrid ESD plus FTRD intervention after submucosal fibrosis was discovered during dissection. R0 resection was confirmed for all the patient, and three months follow up showed no sign of recurrence in four patients out of 5 as one of them underwent surgical resection to treat his SM3 adenocarcinoma. Recent studies reported the same outcome at six months [7]. These results encourage us to find more indications for FTRD. In conclusion, more studies are showing positive results from using ESD combined with FTRD to treat difficult lesions and in particular lesions hiding submucosal fibrosis. This makes it a promising procedure, but guidelines are lacking.

- G29 -

ENDOSCOPIC TREATMENT OF ACUTE CHOLECYSTITIS USING 'HOT AXIOS' STENTING: A CASE SERIES. E. Devolder (1), D. De Wulf (2) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [2] AZ Delta, Roeselare, Belgium, Gastroenterology.

Introduction: Cholecystectomy has been accepted as the gold standard for managing cholecystitis. Nevertheless, some patients are poor surgical candidates due to functional status (underlying comorbidities or older age), late presentation, or anticoagulation therapy. Treatment with antibiotics is the mainstay of management in this population. However, additional source control may be desirable in seriously ill or debilitated patients. At this point, percutaneous gallbladder drainage (PT-GBD) or endoscopic gallbladder drainage (EUS-GBD) may be performed. The use of a lumen-apposing metal stent (LAMS) enables the therapeutic endoscopist to relieve obstruction and provides adequate source control. It has been described in cases as a definitive therapy as well as a bridge to elective cholecystectomy.
Aim: The aim of this case series is to evaluate the indications and also the effectiveness and safety of a LAMS, and more specifically the 'Hot AXIOS' stent.
Methods: In this single center retrospective case series, we report 26 cases of cholecystitis managed with EUS-GBD. The stent facilitates safe and accurate access to the gallbladder under guidance of endoscopic ultrasound (EUS).
Results: In our experience, this innovative technique offers new opportunities. We favor EUS-GBD because of low rates of recurrent cholecystitis and adverse effects, but also because of great comfort and little pain for the patient. EUS-guided gallbladder decompression is minimally invasive and has a high success rate.
Conclusions: The placement of a LAMS could be a safe and effective approach in the management of cholecystitis in selected patients.

- G30 -

MULTIMODAL MASTERY: ENDOSCOPIC MANAGEMENT OF A LARGE ANGIODYSPLASTIC LESION IN A PATIENT WITH SEVERE IRON-DEFICIENCY ANEMIA. L. Debels (1), P. Poortmans (1) / [1] UZ Brussel, Brussels, Belgium, Department of Gastroenterology and Hepatology.

Video Abstract: A 69-year-old male patient with iron-deficiency anemia (Hemoglobin: 5.6 g/dL) characterized by fatigue and shortness of breath, yet without evident blood loss, was subjected to diagnostic gastroscopy and colonoscopy. While gastroscopy yielded no definitive findings, colonoscopy revealed a notable 15mm hyperemic lesion in the caecum, indicative of a large angiodysplastic lesion. Initial treatment involved the application of an over-the-scope clip (OTSC). However, this intervention was complicated by pulsatile bleeding from the lesion through the clip. Subsequent immediate management utilized coagulation forceps, effectively halting the pulsatile hemorrhage. Nevertheless, minimal oozing from the clip's edges persisted. To address this, hemostatic spray was employed as hemostatic and preventive measure against further bleeding. The patient was admitted for close observation considering the complexity and severity of the case. Despite the multi-modal endoscopic interventions, the lesion's intricate nature rendered further endoscopic treatment unfeasible. Therefore, the medical team prepared for a potential shift to interventional radiology should rebleeding occur. This case exemplifies the challenges in managing significant angiodysplastic lesions in the elderly and underscores the importance of a versatile, multi-pronged approach in endoscopic treatment, balancing efficacy with the safety of the patient.

- G31 -

OVERT SMALL BOWEL BLEEDINGS: DIFFERENT APPROACHES FOR DIFFERENT CASE SCENARIOS. M. Fernandez (1), M. Arvanitakis (2) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology, [2] Erasme Hospital, Brussels, Belgium, Gastroenterology.

Video Abstract: Small bowel bleeding (SBB) represents 5-10 % of all GI bleeding cases and is often difficult to diagnose. Although International Guidelines are well-established, different approaches can be proposed depending on the patient's story. Small bowel capsule (SBC) plays a significant role in SBB and can be combined with other imaging procedures such as dynamic contrast-enhanced CT scan before performing enteroscopy. We illustrated SSB issues with three cases: first, a 71-year-old woman with melena and iron deficiency anemia underwent SBC after nonconclusive esogastroduodenoscopy (EGD) and colonoscopy. Significant angiodysplasia was identified at one hour, and an anterograde enteroscopy allowed the treatment with argon plasma coagulation after submucosal injection. Secondly, a 63-year-old woman under anticoagulation for atrial fibrillation presented with melena and arterial hypotension. EGD was normal. CE-CT showed arterial bleeding in the mid-jejunum not found in angiography. An anterograde enteroscopy showed a Dieulafoy ulceration actively bleeding and successfully treated with clips. Finally, a 44-year-old patient presented with a longstanding history of undetermined GI bleeding with hematochezia and previous small bowel resection due to spontaneous perforation. SBC revealed an ulceration five hours after the pylorus. We performed an anterograde enteroscopy that was normal and then the retrograde route in the same session. A 2cm ulceration at 80 cm from the ileocaecal valve was identified and proven to be a lymphoma. In conclusion, SBB can be challenging and require a combination of clinical and biological aspects and endoscopic and imaging investigations to yield the correct diagnosis and, consequently, a suitable treatment.

- G32 -

NOVEL RESECTION TECHNIQUE FOR LARGE PEDUNCULATED POLYPS AND MANAGEMENT OF POST-RESECTION BLEEDING. L. Janssens (1), N. Buttar (1) / [1] Mayo Clinic, Rochester, United States, Gastroenterology.

Video Abstract: Endoscopic management of large pedunculated polyps can be challenging. A detachable snare is a valuable tool to cinch pedunculated polyps but can be limited by its opening size and maneuverability. We describe a novel approach to resect large pedunculated polyps. A 60-year-old woman was found to have a 6-cm polyp on MRI. Biopsy revealed adenoma with low-grade dysplasia. Upper endoscopy was pursued but various attempts to cinch the pedunculated polyp, including a standard detachable snare and endoscopic purse-string suturing, were unsuccessful. A novel, large-diameter detachable snare with a knot was created. A double-channel scope was preloaded with the novel detachable snare, and the knot was held with pin-less biopsy forceps for steering. With this approach, we successfully cinched the peduncle of the polyp. The polyp was debunked until we reached the peduncle, and a standard detachable snare was placed over the peduncle separately, followed by en-bloc resection. Next, arterial bleeding was noted in the resection bed from a large feeding vessel. Cautery was applied to the vessel using avulsion forceps resulting in bleeding cessation. As the resection bed was too large for standard clip placement or over-the-scope clipping, we performed endoscopic suturing to approximate the edges of the resection bed for hemostasis. We demonstrate the use of a customized large-diameter detachable snare to successfully remove a large pedunculated gastric polyp and the management of post-resection bleeding with a combination of avulsion forceps cautery and endoscopic suturing.

- G33 -

HEMORRHAGIC SHOCK IN UPPER GI BLEEDING. A. Bourgeois (1), A. Attar (2), M. Abdessalami (2), V. De Smet (2), A. Carini (3), P. Eisendrath (2) / [1] CHU Saint-Pierre, Brussels, Belgium, Gastroenterology , [2] CHU Saint-Pierre, Brussels, Belgium, Gastroenterology, [3] CHU Saint-Pierre, Brussels, Belgium, Anesthesiology.

Video Abstract: An 82-year-old female patient was admitted to the emergency department with melena and coffee-ground emesis. Clinically, she was hypotensive (50/30 mmHg) and had prolonged capillary refill and pale skin. Her medical history revealed chronic atrial fibrillation treated with acenocoumarol and daily intake of Ibuprofen and Acetaminophen due to a distal fibula fracture which she suffered from four weeks earlier. She did not take proton pump inhibitors. Laboratory findings revealed severe anaemia, disturbed coagulation and acute kidney injury. The Glasgow-Blatchford Bleeding Score was 18 on admission. A diagnosis of upper GI bleeding with hemorrhagic shock was made. Urgent management consisted of fluid resuscitation, IV pantoprazole and transfusion of blood products and coagulation factors. INR was corrected with IV vitamin K. For hemodynamic management, continuous noradrenalin perfusion was initiated. Hereafter, the patient improved hemodynamically facilitating early endoscopic evaluation. Endoscopic evaluation of the upper gastrointestinal (UGI) tract revealed a Forrest IIa ulcer at the lesser curvature. The decision was made to treat the ulcer with Bipolar Electrocoagulation Therapy (BICAP). During BICAP treatment, active bleeding occurred necessitating injection of Adrenalin. Finally, BICAP treatment was pursued, resulting in succesfull treatment of the ulcer.

The patient was admitted to the intensive care unit for further hemodynamic monitoring and treatment. Here, we describe a case of hemorrhagic shock due to UGI bleeding with coagulation disorder. Likely causes include prolonged NSAID intake without gastric protection as well as a supratherapeutic INR following drug-drug interaction of acenocoumarol with acetaminophen and ibuprofen.

- G34 -

HEMOBILIA AFTER ERCP FOR POST-LIVER TRANSPLANTATION ANASTOMOTIC STRICTURE: IS ENDOSCOPIC HEMOSTASIS ALWAYS POSSIBLE TO TREAT HEMOBILIA? G. Losurdo (1), A. Lemmers (1) / [1] Erasme Hospital, Brussels, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology.

Video Abstract: A 55-year-old male patient was admitted for haematemesis lasting less than 24 hours in our Department. He underwent liver transplantation three months before due to acute fulminant hepatitis B infection. However, post-transplantation clinical course was complicated by early biliary anastomotic stricture with jaundice, therefore an endoscopic retrograde cholangio-pancreatography (ERCP) was performed in order to dilate the stricture and a 10-Fr plastic stent was left in place. At the time of admission, a drop of haemoglobin levels (from 7.4 to 6.7 g/dl) was observed. A previously scheduled ERCP was maintained to replace the stent for multiple ones in order to solve the stricture. During the examination, a bulging, pulsatile mass in the bulb was noticed. The plastic stent was still in place, however, after removal, profuse bleeding coming from the papilla was observed. A nasobiliary catheter without further manoeuvres was left in place. An urgent computed tomography revealed a 3 cm pseudoaneurysm of the hepatic artery. Therefore, bleeding control by angiographic embolization of the pseudoaneurysm was attempted, without success. A surgical approach, by ligation of hepatic artery and Kehr drain insertion because of bile duct necrosis was required. However, because of post-surgical left lobe liver necrosis and septic shock occurrence, a salvage liver re-transplantation was scheduled within one month, this time with favourable evolution.

- G35 -

BALLOON TAMPONADE AS INITIAL TREATMENT OF PER PROCEDURAL POST-SPHINCTEROTOMY BLEEDING. S. Ouazzani (1), A. Lemmers (1) / [1] Erasme Hospital, Brussels, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology.

Video Abstract: Acute bleeding following immediately sphincterotomy is not an uncommon complication and occurs up to 9% of ERCP. Habitual treatment consists in diluted adrenaline injection on the bleeding site, coupled with thermal or mechanical methods in case of persistent bleeding. These second-line methods can induce complication as pancreatitis or can be challenging as for clips use because elevator of the duodenoscope. Often an extraction-balloon is used after biliary sphincterotomy for stone extraction. We present here a case of a 67 year old patient who presented a per procedure post-sphincterotomy bleeding. The patient had cholestasis with biliary duct dilation in a context of metastatic pulmonary carcinoma, with sludge in common bile duct. An ERCP with biliary cannulation was indicated. A venous bleeding occurred immediately after sphincterotomy. An extraction balloon was inflated and placed against the bleeding point for 2 minutes allowing bleeding cessation, without acute or delayed rebleeding. During the follow-up, the patient has no recurrent bleeding, nor any other ERCP-related complication. In case of success, this technic could avoid the use of additional devices, reducing procedure cost and time.

- G36 -

ACUTE BLEEDING DURING ENDOSCOPIC SPHINCTEROTOMY. M. Noreillie (1), D. De Wulf (2) / [1] AZ Delta, Belgium, Gastroenterolgy, [2] AZ Delta, Roeselare, Belgium, Gastroenterology.

Video Abstract:
Background: Endoscopic sphincterotmy (ES) is the cornerstone of therapeutic ERCP. Bleeding is one of the most frequent complications of ES. Bleeding can be acute or delayed. An acute bleeding during ES varies between self-limiting and life-threatening bleeding and is occasionally associated with a considerable mortality rate of 0.3%.
Case: A healthy 56-years-old lady presented for ERCP for symptomatic solitary common bile duct stone. **Methods:** We used an Olympus TJF – Q180V endoscope and an Olympus Clevercut3V distal wireguided with Visiglide 2 guidewire, 0,025 inch at the tip. The first two cannulation attempts resulted in pancreatic wire cannulation, so we decided to perform a transpancreatic precut papillotomy and prophylactic placement of a Boston Scientific Advanix 5Fr 5 cm pancreatic stent. A next bile duct cannulation attempt was successful. A normal sized over the wire endoscopic sphinctertomy (with the blended current 20 W cut; 20 W coagulation in the ESG 100 System from Olympus) was done but resulted in a severe arterial bleeding. A stone was extracted using a Olympus Multi -3V Plus extraction balloon over the wire and inflated to 11.5 mm. An attempt to tamponade the bleeding with the extraction balloon was not successful. To maintain position in a bloody situation, the guidewire was kept in place at all time. 6 ml Epinephrine was injected (1:10,000 dilution) around

the bleeder but could not stop the bleeding. A fully covered Boston Scientific Wallflex Biliary Rx stent 10 x 40 mm was placed and could stop the bleeding. We observed a 1 g/dl hemoglobin drop on the next day. Patient could be discharged and no late bleeding occurred. After two weeks both fully covered bile duct and pancreatic stent were retrieved.
Conclusion: Managing acute bleeding during endoscopic sphincterotomy can be challenging. A combination of injection therapy and tamponade with a fully covered stent is used successfully in this case.

- G37 -

ENDOSCOPIC TREATMENT OF PEPTIC ULCER BLEEDING POST GASTRIC BYPASS SURGERY. M. Noreillie (1), D. De Wulf (2) / [1] AZ Delta, Belgium, Gastroenterology, [2] AZ Delta, Roeselare, Belgium, Gastroenterology.

Video Abstract:
Background: Endoscopic treatment of peptic ulcer bleeding after gastric bypass surgery is challenging because of the inability to reach the excluded stomach and duodenum by conventional endoscopy.
Case: A 38-year-old lady with a history of gastric bypass surgery and recently diagnosed acute alcoholic hepatitis on an underlying alcoholic cirrhosis presented with hypovolemic shock due to gastrointestinal bleeding. Conventional upper and lower GI endoscopy were negative for bleeding. Angio CT-scan showed a duodenal bleeding, but interventional angiography failed to stop the bleeding. Persistent bleeding led to polytransfusion, DIC and MOF. The interventional endoscopist was consulted after 7 days in the ICU, where an EDGE procedure was proposed. - Methods Endoscopic ultrasound was performed using an Olympus GF-UCT 180 endoscope and Aloka ultrasound in an intubated and ventilated patient in the endoscopy department. The excludes stomach was easy identified because it contained a large amount of (old) blood. A LAMS Hot Axios (20x10 mm) stent was placed from the gastric pouch. We switched to an Olympus GIF-HQ 190 endoscope for immediate dilation to 20 mm by using a Boston Scientific CRE 18-20 mm balloon. The excluded stomach was entered and cleaned of a large amount of old and fresh blood. A large bulbar ulcer with Forrest classification Ib was observed. Due to the large fibrotic ulcer base and severe clothing disorder, we decided tot perform hemastasis with an Ovesco OTSC 11 mm clip. We could easily pass the LAMS stent with the Ovesco device on the scope. The bleeding stopped and there was no further rebleeding in the next days. Unfortunately, the patient died 6 days later due to a combination of underlying cirrhosis, MOF and polytransfusion. We hypothesize that an earlier EDGE procedure could have prevented polytransfusion and possibly let to a better patient outcome.
Conclusion: Endoscopic treatment of peptic ulcer bleeding with OTSC in gastric bypass patients is feasible using the EDGE technique and should not be delayed in cases of severe bleeding.

- G38 -

MANAGEMENT OF RECURRENT DUODENAL BLEEDING IN ROUX-EN-Y ANATOMY. L. Janssens (1), D. Penrice (1), A. Storm (1), L. Wong Kee Song (1) / [1] Mayo Clinic, Rochester, United States, Gastroenterology.

Video Abstract: The management of duodenal bleeding in patients with Roux-en-Y anatomy can be challenging. Endoscopic Ultrasound-directed transgastric stenting with lumen-apposing metal stent (LAMS) can facilitate access to the duodenum to provide endoscopic hemostasis.
An 83-year-old man with a history of Roux-en-Y gastric bypass presented to the hospital with melena and acute anemia. Initial CT and upper endoscopy did not reveal the bleeding source. Antegrade double-balloon enteroscopy was performed. Evaluation of the pancreaticobiliary limb noted a large (>50 mm) bleeding ulcer in the duodenum treated with epinephrine injection, bipolar probe coagulation, and three through-the-scope clips. Two days later, he had evidence of recurrent bleeding treated by interventional radiology with Gelfoam embolization of an actively bleeding inferior pancreaticoduodenal artery branch. Despite this intervention, the patient continued to have high vasopressor requirements with ongoing melena and dropping hemoglobin. Therefore, the decision was made to perform endoscopic ultrasound-directed transgastric stenting with a LAMS to facilitate duodenal access. First, the remnant stomach was punctured and filled with a mixture of contrast and saline. Next, a 20 x 10 mm LAMS was deployed between the pouch and remnant stomach and was sutured in place using the overstitch device. The gastroscope was then advanced to the duodenum where an ulcer was seen (proximal to the previously treated ulcer) with a spurting hemorrhage. The area was injected with epinephrine and treated with a bipolar probe. Finally, a mixture of cyanoacrylate and lipiodol was injected resulting in hemostasis.

BELGIAN HELICOBACTER AND MICROBIOTA STUDY GROUP (BHMSG)

- H01 -

COMPARISON OF ERADICATION EFFICACY OF 1-WEEK AMOXICILLIN-CONTAINING BISMUTH QUADRUPLE REGIMEN AND 2-WEEK BISMUTH QUADRUPLE REGIMEN FOR H PYLORI WITH CLARITHROMYCIN RESISTANCE-RELATED GENE MUTATION (A2143G). S. Kim (1) / [1] The Catholic University of Korea Seoul St. Mary's hospital, Seoul, Korea (the Republic of), Division of Gastroenterology.

Introduction: In areas where CLA-resistant strains are prevalent, 2-week OBMT (omeprazole, bismuth, metronidazole, tetracycline) therapy is recommended as the first treatment. But, The medication process is inconvenient. If a gene mutation related to CLA resistance is confirmed, 1 week of OAM (omeprazole, amoxycillin, metronidazole) therapy is recommended. The sterilization rate is known to be below 80%.
Aim: We wanted to find out whether OAM+B 1-week therapy can have the same effect as OBMT 2-week therapy.
Methods: Propensity score matching (PSM) was used in a multicenter retrospective analysis. Cases in which OBMT2w or OAM+B1w were administered were selected as positive (A2143G) in CLA resistance-related gene mutation PCR, if there has been no exposure to other antibiotics related to eradication within 1 year. The primary analysis target is the eradication rate, and the secondary analysis target is medication compliance and frequency of side effects
Results: The research period is from October 2019 to May 2023. Helicobacter infection and clarithromycin resistance-related gene mutations were confirmed using PCR and 115 patients with the A2143G mutation were analyzed. Of the 115 patients, a retrospective analysis was performed on 82 patients prescribed a UBT test after taking antibacterial medication, more than 4 weeks had elapsed, and their medical records were faithfully maintained. Among the 82 patients subject to analysis, 51 cases were administered the conventional 2-week bismuth quadruple regimen, and 31 cases were administered the combination therapy of amoxicillin and metronidazole for 1 week as recommended after antibiotic resistance testing. Amoxicillin and metronidazole combination therapy included bismuth three times a day. PSM was performed in both groups for gender, age, and body mass, which are believed to affect the effectiveness of bacterial eradication, and 25 cases were selected in each group after PSM. The distribution of age and gender was not different for the two groups. There was no difference in body mass index between the two groups after PSM. Smoking and drinking tendencies did not differ between the two groups, and the presence or absence of comorbidities, individual comorbidities, and frequency of taking antithrombotic agents such as aspirin did not differ between the two groups. The reason for eradication treatment was atrophic gastritis or H. pylori-infected gastritis including intestinal metaplasia, which accounted for 56.0% to 78.4% of the cases in each group, and there was no difference in the cases of peptic ulcer or neoplasm between the two groups. The effectiveness of eradication therapy was confirmed by UBT performed 4-8 weeks later. In the pre-PSM analysis, the eradication rates of the OBMT2w group and the AOM+B1w group were 70.6% and 77.4%, respectively, in the ITT analysis, and 94.7% and 85.7% in the PP analysis, with no difference in both analyses. In the post-PSM analysis, the eradication rates of the OBMT2w group and the OAM+B1w group were 68.0% and 80.0% in the ITT analysis, and 94.4% and 87.0% in the PP analysis, with no difference in both analyses. Regarding medication compliance, 85.7% and 100% of the OBMT2w and OAM+B1w groups responded that they had taken more than 85% of all medications, respectively. There was no difference between the two groups and also before and after PSM. In the investigation of incidental symptoms, there was no difference in the frequency of incidental symptoms between the two groups. Cases requiring discontinuation of medication occurred in 5.3-5.6% of the OBMT2w group, but did not occur in the OAM+B1w group. However, changes in defecation patterns were common in the OAM+B1w group, with black changes in stool being the main reason. In the pre-PSM analysis, cases complaining of nausea or general weakness were more frequent in the OAM+B1w group, but there was no difference in the post-PSM analysis.
Conclusions: For H. pylori infection with clarithromycin resistance-related gene mutations, the 1-week metronidazole triple regimen with added bismuth showed no difference in eradication rate compared to the conventional 2-week bismuth quadruple regimen. When taking the 1-week metronidazole triple regimen with bismuth added, medication compliance was superior compared to the conventional 2-week bismuth quadruple regimen

BELGIAN INFLAMMATORY BOWEL DISEASE RESEARCH AND DEVELOPMENT GROUP (BIRD)

- I01 -

HISTO-ENDOSCOPIC REMISSION (HEMR) PREDICTS FUTURE RELAPSE IN PATIENTS WITH ULCERATIVE COLITIS AND IS ASSOCIATED WITH LOWER COLECTOMY RISK. M. Lenfant (1), G. De Hertogh (2), J. Sabino (1), B. Verstockt (1), M. Ferrante (1), S. Vermeire (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Pathology.

Introduction: Treating beyond clinical and endoscopic remission, aiming for histological remission, is an aspiring target in ulcerative colitis [UC]. Hence, combined histo-endoscopic endpoints are increasingly being embraced.
Aim: We assessed different degrees of histologic remission in patients with UC and their association with long-term outcomes.
Methods: UC patients achieving endoscopic improvement (Mayo endoscopic score [MES] ≤1) were recruited at colonoscopy. Clinical data were retrospectively collected from medical records. Endoscopies were recorded and biopsies from the most affected segment were collected for histological assessment and RNAseq (in case of MES 0 rectosigmoid biopsies were collected according to previous disease extent). Geboes Score [GS] and the Robarts Histopathology Index [RHI] were determined for each biopsy by two pathologists blinded to the endoscopic scores. Non-histo-endoscopic remission [NHR], histo-endoscopic mucosal remission [HEMR] and histo-endoscopic mucosal normalization [HEMN] were defined as GS ≥2B.1, GS <2B.1 and GS ≤0.1 respectively. Clinical relapse was defined as the need for dose optimization, switching therapy or initiation of corticosteroids during follow-up. Long-term outcomes were analysed using log-rank test and Cox regression (R 4.3.2).
Results: Between 2016 and 2022, a total of 172 UC patients were included. Endoscopic remission (MES 0) was achieved in 104 (60.4%) patients. NHR, HEMR and HEMN were observed in 15 (14.4%), 69 (85.6%), 51 (49.0%) of MES 0 patients and 32 (47.1%), 36 (52.9%), 18 (26.5%) of MES 1 patients respectively. During a median [IQR] follow-up of 2.8 (1.9-3.9) years, 51 (29.7%) patients relapsed, and 7 (4.0%) patients needed colectomy. Relapse- and colectomy-free survival were significantly higher when comparing HEMR to NHR ($p<0.001$ for both). This difference was not observed for endoscopic score (MES 0 vs. 1) or different degrees of histologic remission (HEMN vs. HEMR). The univariate Cox regression showed that histo-endoscopic activity, clinical activity (i.e., patient reported outcomes (PRO-2) for stool frequency or rectal bleeding > 0) and prior advanced therapy failure were associated with an increased risk of relapse. The multivariate Cox regression identified histo-endoscopic activity as the only risk factor for relapse (adjusted hazard ratio [HR]) = 3.01, 95% confidence interval [1.69-5.34], $p<0.001$).
Conclusions: In this cohort of UC patients with endoscopic improvement, 14.4% of MES 0 and 47.1% of MES 1 patients still showed signs of histologic activity (i.e., presence of neutrophils in the lamina propria or epithelium. Histologic remission was a superior predictor of future outcome (relapse, colectomy) when compared to endoscopic remission and showed to be the sole predictor of relapse.

- I02 -

GENETIC DETERMINANTS FOR SMOKING BEHAVIOUR IMPROVE OUR UNDERSTANDING OF SPORADIC VERSUS FAMILIAL INFLAMMATORY BOWEL DISEASE. D. Jans (1), Y. Abakkouy (1), S. Becelaere (1), S. Verstockt (2), S. Vermeire (3), I. Cleynen (1) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Human Genetics, [2] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing (CHROMETA), [3] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Disease, Metabolism and Ageing (CHROMETA).

Introduction: Inflammatory bowel disease (IBD) is influenced by genetic and environmental factors. The latter are often difficult to quantify and may vary over time, unlike genetics.
Aim: Here, instead of looking at actual smoking behaviour, we explored the impact of genetic determinants of smoking behaviour on IBD risk in sporadic and familial IBD.
Methods: We calculated polygenic scores (PRS) for smoking initiation, smoking cessation, age of smoking initiation, and cigarettes per day in 2784 sporadic cases (1700 CD, 1084 UC), 682 non-IBD controls, and 60 multiplex IBD families with ≥3 affected first-degree relatives (FDR) (142 CD, 31 UC and 100 unaffected FDR). PRS were calculated for different p-value thresholds (5e-8, 1e-5, 0.01, 0.05, 0.1, 0.5 and 1), and based on effect estimates of Saunders et al (Nature 2022). Groups were compared using logistic regression. $P<1.43e-3$ was the significance threshold for Bonferroni correction.
Results: Sporadic IBD cases had a higher PRS for smoking initiation than controls (p=4.49e-3), which was driven by the CD cases (p=7.17e-4,). CD cases also showed a trend for a higher PRS for cigarettes per day (p=0.026). In familial cases compared to unaffected FDR, we observed some differences in PRS for smoking, but none survived multiple testing. Comparing familial and sporadic cases, we found that the PRS for age at smoking initiation was higher in familial than in sporadic UC (p=9.09e-4). Familial CD showed a trend towards a lower PRS for age at smoking initiation (p=0.023)

and smoking cessation (p=0.013) than sporadic CD. Familial CD cases are thus more at risk than sporadic CD cases as they genetically tend to start smoking younger, while the opposite is seen for UC. Also, unaffected FDR of UC families showed a lower PRS for age at smoking initiation (p=5.47e-5) than controls, giving them additional protection. The PRS for smoking cessation (p=3.88e-5) and cigarettes per day (p=4.47e-3) was greater in unaffected FDR of mixed families than in controls, while familial mixed cases had a lower cigarettes per day PRS than sporadic cases (p=1.59e-4).
Conclusions: We found that genetic determinants of smoking behaviour are associated with disease risk in familial and sporadic IBD. While CD risk overall is associated with a greater genetic propensity for smoking initiation, the higher risk in families is linked to genetic age at start of smoking. Meanwhile, unaffected FDR of these families are protected through a higher genetic propensity to stop smoking in mixed families, or to start smoking sooner in UC families, compared to population controls. This study improves our understanding of familial vs sporadic IBD, and could help stratify individuals at risk of IBD.

- I03 -

THE ROLE OF HISTOLOGY FOR THE PREDICTION OF CLINICAL RELAPSE IN CROHN'S DISEASE: A SUBSTUDY OF THE STORI COHORT. C. Reenaers (1), D. Enea (2), M. Nachury (3), D. Laharie (4), Y. Bouhnik (5), M. Fumery (6), J. Gornet (7), A. Aurélien (8), R. Altwegg (9), M. de Vos (10), P. Marteau (11), A. Bourreille (12), S. Nancey (13), S. Viennot (14), E. Louis (15), M. Svrcek (2) / [1] CHU Liege, Liège, Belgium, gastroenterology, [2] Hospital Saint Antoine, Equatorial Guinea, Pathology, [3] CHU Lille, France, Gastroenterology, [4] CHU Bordeaux, France, Gastroenterology, [5] institut des MICI, France, Gastroenterology, [6] CHU Amiens, France, Gastroenterology, [7] Hospital Saint Louis, France, Gastroenterology, [8] Kremelin Bicètre, France, Gastroenterology, [9] CHU Montpelier, France, Gastroenterology, [10] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology, [11] Hospital Saint Antoine, Equatorial Guinea, Gastroenterology, [12] CHU Nantes, France, Gastroenterology, [13] CHU Lyon, Lyon, France, Gastroenterology, [14] Clinique de l'Alma, France, Gastroenterology, [15] CHU Liege, Liège, Belgium, Gastroenterology.

Introduction: Deep remission including clinical, endoscopic and biological remission has become the target in the management of Crohn's disease (CD). Although the achievement of histological remission was identified as a predictive factor of favorable outcome in ulcerative colitis, its role has not clearly been established in CD.
Aim: The aim of this work was to study the impact of histological inflammation on the risk of clinical relapse in patients with CD in clinical and endoscopic remission and to study the correlation between histology and endoscopic scores and biomarkers.
Methods: All patients included in STORI (1) were eligible for inclusion. These patients in clinical remission had a fecal calproptectin dosage and a colonoscopy performed at inclusion with CDEIS calculation and 2 systematic biopsies, from the most inflammed area in case of macroscopic inflammation or from an area with previous documented inflammation in case of mucosal healing. Mucosal healing was defined by the absence of macroscopic ulcers. Colonic and ileal biopsies were independently analysed. Different histological scores were calculated by 2 independent pathologists in a central reading process: Robart, Geboes, modified Geboes, Nancy, and DCA-IBD. Histological remission was defined by Nancy=0 ; Geboes ≤ 2 ; modified Geboes of grade 0 ; Robarts ≤ 3, IBD-DCA of C≤ 1 and A=0. Histological response was Nancy≤ 1; Geboes ≤ 3,1 ; Robarts ≤ 9, IBD-DCA of C≤ 2 and A=0. Clinical relapse was prospectively evaluated in the STORI trial and defined by CDAI>250 or CDAI between 150 and 250 with an increase of 70 points during 2 successive weeks compared to the inclusion visit. (1) Louis E et al Gastroenterology 2012;142:63–70
Results: Eighty biopsies (22 ileal and 58 colonic) were available from 76/115 patients included in STORI. Among the 45 patients with mucosal healing, 30 had colonic biopsies, 11 had ileal biopsies and 4 had biopsies in both locations. Among colonic biopsies 68% had histological remission according to Nancy and Modified Geboes scores, 65% according to DCA-IBD and Geboes scores and 71% according to Robarts score. Among ileal biopsies 53% had histological remission according to Nancy score, 47% according to Modified Geboes, Geboes and DCA-IBD scores, and 67% according to the Robarts score. Thirty-five patients (46%) experienced a clinical relapse during the follow-up including 16/45 (36%) and 19/31 (61%) in the group without and with macroscopic ulcers respectively. Histological characteristics and histological scores were not predictive of clinical relapse. In the total cohort (n=76), the CDEIS score was correlated to Nancy (p<0,001, r=0,43), Geboes (p<0,001, r=0,47) and Robarts (p<0,001, r=0,45) scores. Fecal calprotectin was correlated to Nancy (p<0,001, r=0,48), Geboes (p<0,001, r=0,45) and Robarts (p<0,001, r=0,46) scores. The histological scores of Nancy, Robarts and Geboes were highly correlated (p<0,0001 ; r > 0,9).
Conclusions: Although correlated with endoscopy and biomarkers, histology including different histological scores and characteristics, was not predictive of clinical relapse in CD patients in clinical and endoscopic remission. These findings don't support the use of histology in clinical practice to predict clinical relapse in CD.

- I04 -

THE HISTO-ENDOSCOPIC SPECTRUM IN ULCERATIVE COLITIS REVEALS A DISTINCT MUCOSAL TRANSCRIPTOME FOR HISTO-ENDOSCOPIC REMISSION. M. Lenfant (1), G. De Hertogh (1), J. Sabino (1),

B. Verstockt (1), M. Ferrante (1), S. Verstockt (2), S. Vermeire (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [2] KUL - University of Leuven, Leuven, Belgium, Chronic Diseases, Metabolism and Ageing.

Introduction: Aiming for histological remission on top of endoscopic remission, is an aspiring target in ulcerative colitis [UC].
Aim: We investigated the mucosal transcriptional profiles in UC patients with varying depths of histologic activity as compared to healthy controls.
Methods: UC patients with endoscopic improvement (Mayo endoscopic score [MES] 0 or 1) were recruited. Endoscopies were video-recorded and biopsies from the most affected segment were collected for histological assessment and bulk RNAseq (Illumina HiSeq 4000, single read). Geboes Score [GS] was determined by two pathologists blinded for endoscopic scores. The included patients were divided into endoscopic improvement with histologic activity [EIHA] (MES ≤1, GS ≥2B.1) and histo-endoscopic mucosal remission [HEMR] (MES ≤1, GS <2B.1). We distinguished a subpopulation within the HEMR group that we labelled as histo-endoscopic mucosal normalization [HEMN] (MES ≤1, GS ≤0.1). As comparators, 50 healthy individuals [HV] and 50 UC patients with active disease (MES 2-3, independent patients, matched by treatment) [AD] were included. Normalised RNA counts were analysed by principal component analysis [PCA] and differential expression analysis. Genes with a |log2 FC|>1 and a FDR <0.05 were considered as differentially expressed [DEG], and were selected for pathway analyses (R 4.3.2, DEseq2; QIAGEN IPA).
Results: In this study cohort 172 patients were included (Table). PCA analysis showed clustering patterns for each study group (i.e., HV, HEMN, HEMR without HEMN, EIHA and AD; Figure). In particular, separation along the PC1 axis tended to follow the different degrees of histo-endoscopic activity. Interestingly, besides inflammatory and tissue remodeling markers (e.g., DUOX2, MMP 3, CHI3L1) for PC1 and epithelial and metabolic markers (e.g., SLC9A3, LPIN3) for PC2, the gene with the highest variance for both PC1 and PC2 was Aquaporin-8 (AQP8). This gene encodes for a water transporter at the apical surface of the colon, and its mucosal expression level indeed follows a spectrum of histo-endoscopic activity (Figure). Differential expression analyses identified 1261 DEG in HEMN, 1684 DEG in HEMR (not HEMN), 2178 DEG in EIHA, all compared to HV. A total of 1014 overlapping DEG were identified for all these comparisons, being enriched for pathways related to inflammation, metabolic epithelial functions (lipid metabolism, bile acid regulation) and wound healing.
Conclusions: UC patients with histo-endoscopic remission have a mucosal transcriptional profile which significantly differs from that of healthy individuals, even in UC patients whose biopsies appear normal upon histological evaluation. The histo-endoscopic spectrum of the mucosal transcriptome in UC is nicely illustrated by the gene expression of Aquaporin-8 (AQP8).

- I05 -

MUCIN MRNA ISOFORM SIGNATURES AS POTENTIAL NOVEL BIOMARKERS TO EVALUATE DISEASE STATUS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES.

W. Arras (1), B. Oosterlinck (1), A. Jauregui Amezaga (2), M. Somers (2), E. Macken (2), J. De Man (1), B. De Winter (1), A. Smet (1) / [1] University of Antwerp, Antwerp, Belgium, Laboratory of experimental medicine and pediatrics, [2] Antwerp University Hospital, Edegem, Belgium, Gastroenterology and Hepatology.

Introduction: Mucosal barrier dysfunction and aberrant mucin expression are major hallmarks in the pathophysiology of IBD. 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, potentially resulting in progression towards disease. Currently, little attention has been given to the importance of mucin mRNA isoforms in IBD.
Aim: The aim of our study is to investigate the potential of mucin mRNA isoforms as novel biomarkers for the evaluation of IBD activity and subtypes.
Methods: To obtain this goal, RNA was extracted from colonic and terminal ileal biopsies of IBD patients that underwent an endoscopy at the Antwerp University Hospital (UZA). Additionally, patients without a history of IBD undergoing an endoscopy due to a positive iFOBT which show no endoscopic abnormalities, were included as controls. 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 all mucin gene transcripts. Samples were sequenced on the PacBio Sequel platform at the University of Antwerp. The data was analyzed by using the isoseq3-pipeline and additional filtering with SQANTI3 was performed. In total 106 biopsies were sequenced on the PacBio platform. The resulting intestinal mucin transcriptome was merged with the human reference transcriptome. On this combined mucin transcriptome Illumina bulk RNA sequencing data from over 2000 intestinal biopsies (GEO dataset GSE193677) were mapped to determine mucin isoform expression. An external dataset (GEO dataset GSE165512) was used for additional validation. A classification random forest was trained on this data to distinguish inflamed IBD from non-inflamed control patients based on the mucin isoform expression alone.

Results: Overall the model performed well on train and test datasets with AUC between 89.1% and 93.3% but decreased in the external validation to values between 53.9% and 76.8%. Dividing the samples based on disease phenotype greatly increases performance on the external validation dataset (AUC[IBD] 53.9%, AUC[CD] 59.2% and AUC[UC] 76.8%). When only training on ileal biopsies, the model proved to be excellent in distinguishing Crohn's disease patients from controls with an AUC of 91.1%, 89.0% and 74.5% for the train, test and external validation dataset, respectively. Classification of inflamed ulcerative colitis from control patients based on only the biopsies from the distal colon was similar to the latter.
Conclusions: Our machine learning model was able to distinguish Crohn's disease from control patients and ulcerative colitis from control patients based on mucin mRNA isoform expression. In addition, our data suggests that the mucin isoform expression may vary between different regions within the colon.

- I06 -

THE LIPIDOME OF CREEPING FAT IN CROHN'S DISEASE POINTS TOWARDS A HARMFUL MICRO-ENVIRONMENT. S. Verstockt (1), J. Dehairs (2), F. Vanderhoydonc (2), B. Ke (1), I. De Greef (1), J. Sabino (3), M. Ferrante (3), G. Bislenghi (4), A. D'Hoore (4), J. Swinnen (2), B. Verstockt (3), S. Vermeire (3) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism (CHROMETA), [2] KUL - University of Leuven, Leuven, Belgium, Department of Oncology, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Abdominal Surgery.

Introduction: A pathognomonic observation in Crohn's disease (CD) is the existence of mesenteric adipose tissue (MAT) wrapping around the inflamed and fibrotic intestine, so-called creeping fat. The etiology of this phenomenon is unclear, and both a protective and harmful role in disease pathogenesis and progression have been proposed.
Aim: Given this conflicting evidence, we aimed to further unravel the role of creeping fat by extensive profiling of its lipidome.
Methods: We prospectively included 22 CD patients who underwent an ileocecal resection with ileocolonic anastomosis (Table 1). Perioperatively paired adipose tissue samples were collected from 3 locations: (1) creeping fat, (2) MAT close to the proximal unaffected ileum, and (3) MAT far from the diseased ileum, defined as centrally, near the base of the ileocecal artery (Fig. 1A). The lipidome of all 66 samples was profiled by quantitative mass spectrometry (targeted C18 LC-MS/MS and HILIC LC-MS/MS; Lipometrix core KU Leuven). This approach enables the detection of mediator lipids, and membrane and storage lipids, of which the latter group represents more complex chemical structures and thus a higher diversity in classification and number of species. Data analysis and paired Wilcoxon rank- sum tests were performed with Python and R 4.3.2.
Results: Across all CD adipose tissue samples, we detected 38 mediator lipid species, and 456 membrane and storage lipid species. When paired-wise comparing creeping fat with MAT far from the diseased ileum, we observed a significant decrease in 16 lipid mediators ($p<0.05$), namely arachidonic acid (AA), docosahexaenoic acid (DHA), 4 epoxy and 10 hydroxy mediator lipids; with hydroxy mediator X being the top downregulated in creeping fat (fold change (FC)=-2.11, $p=0.0003$) (Fig. 1B). While AA and DHA are (semi)-essential fatty acids and function as precursors, the other 8 decreased lipids in creeping fat are known to be anti-inflammatory, and 3 (incl. mediator X) are also anti-fibrotic. The lipid mediator profile of MAT close to the proximal unaffected ileum was similar to that of creeping fat, except for a pro-inflammatory lipid being increased in creeping fat (FC=2.30, $p=0.004$) (Fig. 1B). Lastly, when evaluating the membrane and storage lipid abundances both at species level (sum notation; fatty acyl composition) and at class level, no paired-wise differences among the three adipose tissue locations were found ($p>0.05$).
Conclusions: In this pilot lipidomics study, we did not observe any changes in storage or membrane lipids in creeping fat as compared to paired unaffected MAT. In contrast, a decrease in anti-inflammatory and anti-fibrotic lipid species along with an increase in a pro-inflammatory species points towards a harmful microenvironment within creeping fat.

- I07 -

STUDY OF THE ROLE OF THE EPITHELIUM IN THE INITIATION AND PROGRESSION OF INTESTINAL FIBROSIS IN ULCERATIVE COLITIS. M. Stepniak (1), P. Adam (2), C. Salée (3), J. Loly (2), S. Vieujean (2), C. Reenaers (2), F. Fonzé (2), C. Massot (2), C. Coimbra Garcia Marques (4), E. Decker (4), N. Blétard (4), P. Delvenne (4), S. Speca (5), E. Louis (2), M. Meuwis (2) / [1] University of Liege, Liège, Belgium, Translational Gastroenterology, [2] Liege University Hospital, Liege, Belgium, Gastroenterology, [3] Liege University Hospital, Liege, Belgium, Gastroenterology, [4] Liege University Hospital, Liege, Belgium, Anatomo-pathology, [5] University of Lille, Inserm, CHU Lille, France, Infinite unit.

Introduction: Intestinal fibrosis in Ulcerative colitis (UC) is poorly studied whereas pathological fibrosis involves extracellular matrix (ECM) accumulation and/or muscularis mucosae thickening (in ~100% of UC surgical specimen with chronic injury and not with active inflammation). The mucosa of UC may reach a level of activation leading to

proinflammatory cytokines and profibrotic factors (TGF-β) release, the induction of Fibroblast to Myofibroblast transition (FMT) (α-smooth muscle actin +) leading to excessive ECM deposition. Indeed, myofibroblasts derive from epithelial cells trough epithelial to mesenchymal transition (EMT), proliferation and FMT. The mechanism switch between repair and fibrosis remain unknown while its understanding could offer anti-fibrotic therapeutic targets. The Endoplasmic reticulum (ER) stress and chronic inflammation have been shown increased in CD stricture's epithelium. The response to ER stress involves production of chaperones, transcription factors, the unfolded protein response (UPR), apoptosis and EMT. Anterior gradient protein homolog 2 (AGR2) is such an UPR ER chaperone protecting from EMT and presenting paracrine effects promoting fibroblast migration and FMT. Blockade of AGR2 or other factors involved in ER stress response produced by the epithelium in IBD might be of interest as new therapeutic target.
Aim: Our objective is to better understand the role played by the epithelium in UC intestinal fibrosis initiation and progression. We aim to develop a model of apical out organoid showing a profibrotic phenotype and to characterise the response of such inverted organoids derived from UC samples.
Methods: Apical-out organoids, derived from stem cells of patients undergoing surgeries or mucosectomies were characterized by proliferation (Ki67, OLMF4, LGR5) and differentiation markers (AGR2, MUC2, E-Cadherin, Villin1, Chromogranin A) by RT-q-PCR and by histology for polarity inversion. Differentiated organoids were treated transiently by Tunicamycin (Tm) at increasing doses (0-10 µg/mL). The profibrotic phenotype was obtained after a recovery phase taking place after ER stress induction and media change. This involves EMT markers detection on organoids materials (Villin1 vs E-Cadherin, ACTA2), as well as ER stress (BiP, AGR2, CHOP, sXBP1) by WB, RT-q-PCR or immunofluorescence (IF) imaging. The profibrotic capacities of organoids to produced paracrine drivers under such induction include extracellular AGR2 and functional assays on primary intestinal fibroblasts. These undergo FMT (increase in α-SMA by IF) after exposure to preconditioned organoids media collected during the recovery phase for selection of the best timing. Investigations of 2,5 Di-Tert-Butyl-P-Benzoquinone (TuBHQ), another ER stressor, is ongoing.
Results: Three cellular architecture models were tested: basal-out, apical-out organoids. The apical-out organoid showed a self-differentiating propensity upon complete inversion with KI67 (2 fold decreased in proliferation apical-out compared to basal-out organoids). MUC2, Vill1, E-Cadherin, Vimentin, Chromogranin A and AGR2 displayed heightened expression levels in inverted organoids (2.26 / 1.87 / 1.89 / 3.34 / 1.55 respectively). Differentiation was confirmed by higherfold changes for Muc2 compared to proliferation phase: 3.67x for Apical-out , 7.07x for 2D Monolayer and 93.67x for basal-out oragnoids respectively. BiP, CHOP, sXBP1 showed no significant variation across the three models under basal condition. Histological analysis confirmed morphological disparities: Inverted organoids, outwardly oriented apical pole facilitating mucus drainage in contrast to, the basal-out model with mucus retention within goblet cells and the organoid lumen. Dose-response investigations done on inverted organoids utilizing Tm (1, 2, 4, 6, 10µg/mL) or TuBHQ (10, 20, 40, 60, 80µM) showed the release of eAGR2 into culture media (WB) without detectable cell lysis (GAPDH and B-actin negative). Analyses of cell extracts revealed the presence of AGR2 along with BiP itself with a positive Tm dose correlation. Tm increasing concentrations (1 to 6µg/mL) induced ER stress markers increases (fold change mean of 5 for BIP, sXBP1, CHOP and AGR2). Functional assessments on fibroblasts using recovery media, showed increases in α-SMA and morphological FMT changes for the Tm doses of 2/4/6µg/mL with an optimum at 2µg/mL. The recovery time after Tm stress showing highest eAGR2 release in the absence of cell mortality was 32 hours.
Conclusions: The characterization of apical-out organoids showed all the expected characteristics: architecture, morphology, as well as self-differentiations. The profibrotic phenotype using Tm induction and apical-out polarity organoids have been optimized and comparison with TuBHQ optimum is pending. Our biobank includes IBD and healthy controls enabling further multi-Omic comparisons of factors produced by organoids induced to a profibrotic phenotype.

- I08 -

TWIST1-MEDIATED FAP FIBROBLASTS DRIVES FIBROSIS IN CROHN'S DISEASE. B. Ke (1), S. Abdurahiman (1), B. Verstockt (1), F. Biscu (1), G. Zanella (1), A. Zouzaf (1), L. van Baarle (1), V. De Simone (1), M. Stakenborg (1), S. Santhosh (1), S. Verstockt (1), G. De Hertogh (2), S. Vermeire (1), G. Matteoli (1) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Pathology.

Introduction: Stricturing Crohn's disease (CD) is a distinct clinical phenotype, characterised by the development of fibrotic strictures within the GI tract. These strictures result from chronic inflammation, leading to the accumulation of collagen and scar tissue, causing narrowing of the affected intestinal segments. Due to a lack of anti-fibrotic medication, up to 70% of patients with CD will require surgery in their lifetime, while up to 40% of patients need repetitive resections within 10 years.
Aim: The goal is to uncover novel molecules and pathways involved in the pro-fibrotic actions of fibroblasts during chronic intestinal inflammation, potentially paving the way for innovative therapeutic targets to prevent or treat fibrotic complications in patients with CD.
Methods: To understand inflammation-induced fibrosis, full-thickness ileal punch biopsies from CD patients (n=10) and colorectal cancer (CRC) patients (n=5) undergoing ileocecal resection (ICR), were profiled using single-cell RNA

sequencing (scRNA-seq) on the 10x Genomics platform. Flow cytometry was performed to confirm scRNA-seq findings. Intestinal fibroblasts were cultured in the presence of NicheNet-predicted cytokines or supernatant of FACS-sorted myeloid cells. To confirm the pro-fibrotic role of TWIST1 in fibroblasts, both Harmine (TWIST1 inhibitor)-treated wild-type mice and COL1A2Cre x TWIST1fl/fl mice were subjected to chronic dextran sulphate sodium (DSS)-induced colitis.
Results: Using scRNA-seq, we identified a specific subset of FAP-expressing fibroblasts enriched in fibrotic surgical CD specimens. Flow cytometry confirmed a significant increase of these cells in the inflamed and stenotic ileum, compared to proximal uninflamed ileum and unaffected control ileum from CRC patients undergoing ICR. Computational methods identified TWIST1 as a key transcription factor, mediating fibroblast activation and extracellular matrix (ECM)-regulatory phenotypes. Myeloid cell-derived inflammatory signals were predicted to induce this specific fibroblast activation, resulting in collagen deposition and tissue fibrosis. Intestinal fibroblasts cultured with inflammatory monocyte supernatant or pro-inflammatory cues expressed higher levels of TWIST1, FAP, and COL3A1. After inhibiting TWIST1 with Harmine, collagen expression and ECM accumulation were decreased in fibroblasts. In addition, in chronic DSS colitis, wild-type mice treated with Harmine showed a reduction in collagen deposition. COL1A2Cre x TWIST1fl/fl mice showed improved disease activity, compared to their littermate controls.
Conclusions: Our findings suggest that TWIST1 serves as a central mediator in the activation of fibroblasts, promoting excessive collagen deposition in ileal CD. Targeting TWIST1 may reduce tissue remodelling and prevent fibrosis in CD.

- I09 -

QUALITY OF CARE FOR PATIENTS WITH INFLAMMATORY BOWEL DISEASES: DEVELOPMENT AND VALIDATION OF A BELGIAN QUALITY INDICATOR SET. L. Fierens (1), C. Liefferinckx (2), J. Sabino (3), E. de Dycker (3), V. Wambacq (2), K. Vanhaecht (4), F. Rademakers (5), P. Bossuyt (6), F. Baert (7), D. Baert (8), M. Ferrante (3) / [1] Kliniek Sint-Jan, Brussel, Belgium, Translational Research in Gastrointestinal Disorders (TARGID), Department of Chronic Diseases and Metabolism (CHROMETA), [2] CUB Hôpital Erasme, Belgium, Department of gastroenterology, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [4] KUL - University of Leuven, Leuven, Belgium, Department of Public Health and Primary Care, [5] KUL - University of Leuven, Leuven, Belgium, Faculty of Medicine, [6] Imelda General Hospital, , Belgium, Imelda GI Clinical Research Centre, [7] AZ Delta, Roeselare, Belgium, Department of Gastroenterology, [8] AZ Maria Middelares, Ghent, Belgium, Department of Gastroenterology.

Introduction: Quality indicators are standardized, evidence-based measures of health care quality, categorised as structure (to assess the setting of care), process (to assess whether actions indicating high-quality care are undertaken during service provision) or outcome indicators (provide information about whether healthcare services help people stay alive and healthy). Several quality indicator sets have been developed to standardise, measure and optimise IBD care.
Aim: Our aim was to develop and validate a set to assess IBD care in Belgium and to select a subset of indicators with room for improvement that can be used to implement and improve care in clinical practice.
Methods: The importance of 221 quality indicators (49 structure, 135 process and 37 outcome) identified through literature was scored on a 10-point Likert scale in a two-round modified Delphi exercise by IBD experts. In a third round, the experts indicated and ranked their top 10 indicators with most room for improvement benefitting the patient in the Belgian healthcare system to agree on an improvement subset. In parallel, patient perspectives were collected through two linguistic patient focus groups, one in Flemish (6 participants) and one in French (4 participants). A final consensus meeting was organised to discuss 1) the patient perspectives gained through the focus groups, 2) the results of two Delphi scoring rounds and 3) the results of the additional ranking round. Indicators scoring $\geq$7 by $\geq$80% of the participants during the second scoring round, or based on agreement during the consensus meeting, were included in the final set.
Results: Thirty-two experts (11 IBD nurses and 21 clinicians including 2 paediatricians) participated in all three voting rounds, of which 19 also participated in the consensus meeting (6 IBD nurses and 13 IBD clinicians including 2 IBD paediatricians). In total, 199 quality indicators were agreed upon to assess IBD care in Belgium (41 structure, 123 process and 35 outcome). Eighteen (3 structure, 14 process and 1 outcome) were retained in the improvement subset, related to patient characteristics, endoscopy guidelines, infection prevention, steroid use, the IBD care team, services provided in the IBD clinic, the documentation of patient characteristics, the care pathway and the monitoring of disease activity. The decision to include the latter five themes was driven by the importance to patients, which was evident from the patient focus groups.
Conclusions: An evidence and consensus based set of quality indicators was developed and validated - including an improvement subset - allowing Belgian IBD centres to evaluate quality of provided care, set up quality improvement projects and potentially launch a benchmarking study.

- I10 -

PATIENT PREFERENCES FOR INFLAMMATORY BOWEL DISEASE TREATMENTS: A EUROPEAN SURVEY USING A DISCRETE CHOICE EXPERIMENT. E. Schoefs (1), R. Janssens (1), Á. Gutiérrez-Vargas (2), M. Ferrante

(3), J. Sabino (3), B. Verstockt (3), L. Avedano (4), M. De Rocchis (4), M. Sajak-Szczerba (4), R. Saldaña (4), N. Straetemans (5), M. Vandebroek (2), S. Vermeire (3), I. Huys (1) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Pharmaceutical and Pharmacological Sciences, [2] KUL - University of Leuven, Leuven, Belgium, Faculty of Economics and Business, [3] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology, [4] EFCCA, Belgium, European Federation of Crohn's & Ulcerative Colitis Associations, [5] AZ Vesalius Tongeren, Tongeren, Belgium, Department of Gastroenterology.

Introduction: As the therapeutic landscape for inflammatory bowel disease (IBD) continues to expand, there arises a need to understand how patients perceive and value the attributes associated with both current and emerging treatments.
Aim: This European patient preference study aimed to quantify IBD patients preferences for treatment and disease-related attributes.
Methods: A survey incorporating a discrete choice experiment (DCE) comprising 14 attributes with a partial profile design was disseminated among IBD patients. The survey design was informed by a prior literature review, qualitative research with patients, and expert discussions. Multinomial logit models were used to estimate DCE attribute weights and assess potential interactions.
Results: A total of 1272 IBD patients across 37 countries completed the survey (Crohn's disease=51.3%, Female=69.3%). All parameters had the expected negative signs, meaning that the side effects or negative disease related outcomes in the survey had a negative impact in the patients' utility. Additionally, they were significant predictors ($p<0.05$) of patient choices. Among the different attributes, the severity of abdominal pain and cramps (11.35%) was considered the most important attribute, followed by urgency and pain of having to go to the toilet (11.91%), and severity of fatigue (10.62%). The lowest importance was assigned to the treatment mode of administration (2.56%), onset of action (3.22%), and endoscopic disease activity (3.57%). Differences in patient's attribute weights were found between patients with Crohn's disease and ulcerative colitis, with the former attaching more value to frequency of having to go to the toilet ($p<0.01$), urgency and pain of having to go to the toilet ($p<0.001$), risk of surgery ($p<0.001$), and physical changes ($p<0.01$). Interactions with age in the model showed that older patients attached less importance to treatment and disease-related attributes. Furthermore, females attached more value to severe infections ($p<0.001$), physical changes ($p<0.001$), and skin problems ($p<0.01$). Some differences in preferences of patients in Northern, Eastern, Southern, and Western Europe were identified, with for example patients in Western Europe attaching more value to fatigue ($p<0.001$), psychological impact ($p<0.001$), sleeping problems ($p<0.001$), and skin problems ($p<0.001$) compared to patients in Eastern Europe.
Conclusions: Gastrointestinal problems were considered very important to IBD patients next to other quality of life-related attributes affecting IBD patients' physical, mental, and psychological health such as fatigue, sleeping problems and risk of surgery. Noteworthy, characteristics that distinguish the different treatments from each other (such as mode of administration and onset of action) seem less important to patients. Observed differences in patients preferences as revealed in the DCE emphasize the imperative role of shared decision making in treatment selection.

- I11 -

EARLY BIOLOGICAL USE IN A BELGIAN, PROSPECTIVE INCEPTION COHORT OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE: THE PANTHER COHORT. S. Verstockt (1), E. Glorieus (2), M. De Wolf (3), M. Lenfant (1), M. Barbaraci (3), J. Sabino (4), M. Ferrante (4), J. Geldof (2), B. Verstockt (4), D. Laukens (5), I. Cleynen (6), L. Vandermeulen (3), T. Lobaton (2), S. Vermeire (4) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism (CHROMETA), [2] University Hospital of Ghent, Belgium, Department of Gastroenterology, [3] University Hospital of Brussels, Brussels, Belgium, Department of Gastroenterology and Hepatology, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [5] Ghent University, Ghent, Belgium, Department of Internal Medicine and Pediatrics, [6] KUL - University of Leuven, Leuven, Belgium, Department of Human Genetics.

Introduction: The growing number of advanced therapies has revolutionized the management of inflammatory bowel disease (IBD). Although early use of biological therapies is associated with better long-term outcomes, no data exist for the Belgian population.
Aim: To this end, we evaluated treatment patterns in biological use and persistence in a Belgian inception cohort.
Methods: The PANTHER (Prognostic biobANk of paTients witH Early cRohn's or colitis) cohort consists of adult IBD patients recruited in 3 Belgian IBD referral centres. Patients are included within 3 months after diagnosis and are naïve for immunosuppressives and biologicals, and without previous IBD-related surgery. Treatment use and outcome data are prospectively collected, and time trends for biological use were analysed using log-rank tests and Cox regression (R 4.3.2).
Results: Between 2015 and 2023, a total of 473 newly diagnosed IBD patients were recruited, of whom 270 (57%) were diagnosed with Crohn's disease (CD), 199 (42%) ulcerative colitis (UC), and 4 (1%) IBD type unclassified (Table 1). During a median (IQR) follow-up of 2.6 (1.3-4.3) years, 64 patients (14%) required surgery (n=10 colectomy; n=54 ileocecal/small bowel resection); and 250 patients (53%) received biological therapy within the 1st year after diagnosis. Most patients were treated with anti-TNF (CD 67%; UC 55%) as first-line biological, followed by anti-integrins (CD

24%; UC 43%) and anti-IL12/23 (CD 9%; UC 2%). Time series analysis showed a significant increase in biological use within the 1st year after diagnosis when comparing patients diagnosed between 2015-2017 (44%) to those between 2018-2020 (57%), and to 2021-2023 (66%) (p=0.03) (Fig. 1A). Factors associated to this early biological use were younger age (HR=0.99 [95%CI: 0.98-0.99]), a diagnosis of CD (HR=2.2 [95%CI: 1.6-2.8]); and perianal disease in CD (HR=2.8 [95%CI: 1.8-12.8]). Within this early biological exposure group, 26 patients (10%) needed a resection later on. Therapy persistence over time was higher with early exposure rates in patients diagnosed in 2021-2023 (82%) and 2018-2021 (71%), as compared to 2015-2017 (63%) (p=0.08) (Fig.1B). The mode-of-action of first-line biological did not show any association with persistence (HR=1.0 [95%CI: 0.4-3.0]), while a UC diagnosis did (OR=1.6 [1.1-2.6]). Overall, only 26% of patients had to switch to a second-line, with a switch [anti-TNF > anti-IL12/23] being the most frequent in CD (50%); and from [anti-TNF > anti-integrins] (46%) or vice versa (40%) in UC.
Conclusions: In this Belgian inception cohort, two thirds of patients are currently initiated with biological therapy within the first year after diagnosis. This increased biological use is associated with high therapy persistence rates of >80% after a median follow-up of 1.5 years, and with low rates of surgical resections.

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AGE-RELATED PATTERNS IN BIOLOGICAL THERAPY USE AND SURGERY AMONG IBD PATIENTS: INSIGHTS FROM THE BELGIAN PANTHER COHORT. J. Celis (1), M. Truyens (2), S. Verstockt (3), E. Glorieus (4), M. de Wolf (5), M. Lenfant (3), M. Barbaraci (5), J. Sabino (3), M. Ferrante (3), J. Geldof (4), B. Verstockt (6), D. Laukens (7), I. Cleynen (8), L. Vandermeulen (5), S. Vermeire (9), T. Lobaton (4) / [1] Universiteit Gent, Gent, Belgium, Internal medicine and pediatrics, [2] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology, [3] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism (CHROMETA), [4] University Hospital of Ghent, Belgium, Department of Gastroenterology, [5] University Hospital of Brussels, Brussels, Belgium, Department of Gastroenterology, [6] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [7] Ghent University, Ghent, Belgium, department of Internal Medicine and Pediatrics, [8] KUL - University of Leuven, Leuven, Belgium, Department of Human Genetics, [9] KUL - University of Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Inflammatory bowel diseases (IBD) are predominantly diagnosed during the second to third life decade. However, the disease may manifest itself at any age and current understanding of differences in clinical presentation and therapy use among age groups is still limited.
Aim: We aimed to analyse age-related patterns in biological and surgical treatment among patients with IBD.
Methods: This study utilized data from the PANTHER cohort, a prospective Belgian inception cohort including 473 adult patients with IBD from 3 Belgian referral centres. Patient inclusion took place from 2015 to 2023. Patients were categorized into groups based on the age at diagnosis: 'young adult-onset' (18-39 years), 'adult-onset' (40-59 years), and 'elderly-onset' (60 years). Baseline characteristics and treatments were analysed using Chi square, Mann-Whitney U tests, log-rank tests and/or Cox regression in SPSS.
Results: Of the patients included, 71.5 % were diagnosed at 18-39 years, 21.2% at 40-59 years, and 7.2% at 60+ years. No significant differences were found between age groups (young adult-onset, adult-onset and elderly-onset patients) in terms of IBD typeCD diagnosis (Crohn's disease (CD): 59.7% in the young adult-onset patients, , 54.6% in adult-onset patients, and 45.4% in elderly-onset patients, P=0.256), female gender (%Female: 46.2%, 50.5%, and 42.4% in each age group, P=0.8), median follow-up duration (2.8 years (IQR [1.3;4.3]) in 18-39 age group, 2.3 years (IQR [1.2;4.2]) in 40-59 age group, and 2.1 years (IQR [1-3.7]), P=0.35), and smoking status (17.4%, 19.6%, and 24.2% per age group, P=0.603). No significant differences were found in Montreal classification. In the elderly group, small bowel Crohn's disease (CD) CD (L1 location) was numerically more prevalent, whereas perianal disease and extensive ulcerative colitis (E3) was numerically less common (although all not statistically significant). Use of biologics differed significantly across age groups, in the 18-39 years age group, 65.8% used biological therapy, decreasing to 45.3% in the 40-59 year age groups and 54.5% in those over 60, a significant difference (P<0.001) with highest uptake in young-adult onset patients (65.8%, P<0.001). Significant differences were found in selection of first biologic, anti-TNF was most commonly used in the youngest group (42.7 %), whereas vedolizumab (19.1%) and ustekinumab (3.6%) less frequent; this trend was significantly different across age groups (P=0.002). Time to initiation of a biological was earlier in the youngest cohort (P=0.002). Cox regression analysis revealed that older age at diagnosis (HR 0.987, 95%CI [0.98;0.996], P=0.006), UC (HR 0.495, 95%CI [0.50;0.39], P<0.001) and centre of follow-up (Brussels vs Leuven: HR 0.663, 95%CI [0.4;1], P=0.048) were associated with a lower risk of biological initiation. When analysing CD separately, independent risk factors associated with biological use were perianal disease (HR 2.26, 95%CI [1.6;3.2], P<0.001), L3 (HR 1.85, 95%CI [1.3;2.6], P<0.001,) and L4 (HR 12.7, 95%CI [1.6;98.7], P=0.015,) location (compared to L1 location). In UC patients, E2 (HR 7.9, 95%CI [2.8;22.4], P<0.001) and E3 (HR 6.9, 95%CI [2.4;19.3], P<0.001) were related to earlier use of biologics. During follow-up, 19% of CD and 5.1% of UC patients required IBD-related surgery. Univariate analysis showed a higher need for surgery in younger patients (P=0.042), however, this difference was no longer significant when analysing CD (P=0.272) and UC (P=0.09) patients as separate groups.

Conclusions: Analysis of the PANTHER Biobank reveals significant age-related variation in the administration of biological therapies among IBD patients.

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UPTAKE AND OUTCOME OF TREATMENT WITH THE GLP-2 ANALOGUE TEDUGLUTIDE FOR SHORT BOWEL SYNDROME WITH INTESTINAL FAILURE IN BELGIUM. T. Vanuytsel (1), A. Ballarin (2), H. De Schepper (3), K. Geboers (1), A. Hadefi (2), D. Hermans (4), I. Hoffman (5), K. Huysentruyt (6), N. Lauwers (1), V. Els (7), C. Vercauteren (8), L. Wauters (1), M. Arvanitakis (2) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Leuven Intestinal Failure and Transplantation (LIFT), [2] Hopital Erasme, ULB, Belgium, Gastroenterology, [3] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology, [4] UCL Saint Luc, Brussels, Belgium, Pediatric Gastroenterology, [5] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Pediatric Gastroenterology, [6] UZ Brussel, Brussels, Belgium, Pediatric Gastroenterology, [7] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Pediatric Gastroenterology, [8] UZ Brussel, Brussels, Belgium, Pediatric Surgery.

Introduction: Short bowel syndrome (SBS) accounts for the majority of patients with chronic intestinal failure (IF), defined by a reduced absorptive capacity of the gastrointestinal tract, below the minimum to sustain life and growth in case of children, necessitating parenteral support (PS). Until recently, the therapeutic options for chronic IF due to short-bowel syndrome (SBS-IF) were largely limited to dietary measures and off-label use of anti-secretory therapy and anti-motility agents. It is only since the advent of the glucagon-like peptide 2 (GLP-2) analogues that the disease course of SBS can be modified significantly. Teduglutide, the only marketed GLP-2 analogue is available in Belgium since mid-2021.
Aim: In the current study we aimed evaluate the treatment uptake, response and adverse effects in Belgium in the first two years after market access.
Methods: A prospective study was set up in the 7 Belgian centers of the RIZIV/INAMI convention for home parenteral support who can prescribe teduglutide. Data were entered in an electronic case report form system (eCRF) by each study site. In patients in whom treatment was already started at the time of ethics approvaldata could also be entered retrospectively. Investigated characteristics include demographics, anatomy subtype (type 1: end-jejunostomy; type 2: jejunocolonic anastomosis), PS volume at the start of the treatment and at predetermined intervals and adverse events. Response was defined as ≥20% PS reduction at 6m (type 1) and 12m (type 2). All patients or their parents provided informed consent prior to data entry in the eCRF. Data are shown as median (range) unless specified otherwise. Differences in PS volume at six months were compared using Wilcoxon matched pair signed rank testing.
Results: Between June 2021 and June 2023 16 patients of whom 11 were adults (7 (64%) female; 56 (25-71) years) and 5 were children (1(20%) girl; 6 (4-12) years) were treated with teduglutide. The etiology of SBS in adults was mainly resections in the context of Crohn's disease (45%) and mesenteric ischemia (36%), while necrotizing enterocolitis was the main etiology in children (60%). Most of the patients (11/16 (69%)) had a type 1 anatomy with the other 5 patients (31%) having a type 2 anatomy. The median duration since last intestinal resection was 55 (12-165) months in adults and 41 (26-90) months in children. In adult patients with at least 6 months of treatment (n=8), weekly PS requirements changed from 12.8 (3-35) L/week at baseline to 5.8 (1-24) L/week at week 24 (p=0.03 vs. baseline) and 4.8 (0-14) L/week at week 52 (n=4). One adult patient with type 2 anatomy weaned off PS completely at week 38 after starting teduglutide, which was continued afterwards. Days with PS changed from 7 (3-7) days per week at baseline to 5 (1-7) days per week at week 24 (n=8) and 3.8 (0-7) days per week at week 52 (n=4). Response criteria were fulfilled by 4/5 patients with type 1 and 2/2 patients with type 2 anatomy. In children with at least 6 months of treatment (n=5; all patients), weekly PS needs changed from 9 (5.7-16.4) L/week at baseline to 7.7 (2.3-13.3) L/week at week 24 (p=0.13) and 5.2 (1-10.5) L/week at week 52 (n=3). PS days per week changed from 7 (7-7) days per week at baseline to 7 (3-7) days per week at week 24 (n=5) and 6 (3-7) days per week at week 52 (n=4). All patients fulfilled response criteria. Four patients experienced mild injection site reactions. All adult patients and 3 out of 5 pediatric patients reported some degree of abdominal pain and nausea, which was mostly mild. One adult patient underwent an adhesiolysis because of obstruction 19 weeks after starting teduglutide, which was assessed as a related adverse event. Two adult patients were hospitalized because of biliary complications (cholecystolithiasis and cholangitis). Teduglutide was stopped in two adult patients after 30 and 6 weeks of treatment because of cholangitis and severe nausea with loss of appetite and weight loss respectively.
Conclusions: Teduglutide is the first disease-modifying treatment in SBS with IF, with a clear benefit in terms of PS reduction in adults and children in Belgium. Nevertheless, adverse effects are common of which intestinal obstruction and biliary complications are the most serious, which should be discussed at the start of the treatment.

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RADIATION EXPOSURE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN A BELGIAN TERTIARY REFERRAL CENTRE. T. Jorissen (1), L. Fierens (2), H. Bosmans (3), B. Verstockt (4), J. Sabino (4), S. Vermeire (4), D. Vanbeckevoort (3), M. Ferrante (4) / [1] KUL - University of Leuven, Leuven, Belgium, Faculty of Medicine,

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Introduction: Radiological imaging plays an important role in diagnosis and follow-up of patients with IBD. Due to the progressive character of the disease, repeated imaging may be necessary. A cumulative effective dose (CED), meaning the total diagnostic radiation received, of 75 mSv is often described as the risk level one needs to try not to exceed. However, data on cumulative exposure are limited in IBD.
Aim: In this retrospective study, we analysed the cumulative radiation exposure of patients with IBD in a Belgian tertiary referral centre.
Methods: Electronic health records (EHRs) from all IBD patients followed at the tertiary referral centre between January 1st 1990 and December 31st 2021 were searched for examinations with radiation exposure and received doses in house or in any of 27 collaborating Nexuz hospitals working with the same EHR. Both the annual effective dose (AED) and CED were calculated. A sub-analysis of patients diagnosed after January 1st 2007 was performed, as detailed radiation doses were maintained prospectively from that date onwards.
Results: In total, 3429 IBD patients were included. The median (IQR) AED was 0.39 (0.01-1.66) mSv/year, and was higher in patients with CD than in patients with UC [0.58 (0.01-1.81) vs. 0.17 (0.01- 1.24) mSv/year, p=0.028]. During the first 20 years after diagnosis, the median received CED were found higher in patients with CD than UC (p<0.01). In 5.5% of patients, a CED ≥75 mSv was reached after a median (IQR) of 24 (13-34) years of follow-up. Sub-analysis of 1633 patients diagnosed after January 1st 2007 showed a median (IQR) AED of 0.44 (0.01- 2.12) mSv/year, again higher in patients with CD than in patients with UC [0.82 (0.02-2.38) mSv/year vs. 0.12 (0.01-1.47) mSv/year respectively, p=0.040]. Here, 3.3% patients reached a CED ≥75 mSv during a median (IQR) of 9 (6-12) years of follow-up. Most common reasons for high radiation exposure were comorbidities like malignancy and postoperative complications. Chart review by an IBD expert showed that the indication for most of these examinations was appropriate and that no alternative examination was available in a timely manner.
Conclusions: Up to 5.5% of patients with IBD were exposed to a CED of ≥75 mSv. Although most decisions to perform imaging with radiation exposure were appropriate, vigilance for unconsidered and excessive imaging should be maintained.

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LIMITED LONG-TERM EFFICACY OF CORTICOSTEROIDS IN MICROSCOPIC COLITIS EMPHASIZING THE NEED FOR ADVANCED THERAPIES.

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Introduction: Microscopic colitis (MC) is a chronic inflammatory bowel disease, characterized by chronic watery diarrhea, and consisting of 2 subtypes: collagenous (CC) and lymphocytic (LC) colitis. It mainly affects middle-aged adults, although it can occur at any age. The only approved therapy is budesonide, preferably administered in a tapering regimen given the high relapse rates. However, little is known about the long-term natural history of the disease.
Aim: We aimed to asses the long-term natural history of MC in a large Belgian single center series. To review which secondline therapies are adequate when mainstream therapy appears to be insufficient.
Methods: All adult patients diagnosed with MC after clinical and histological assessment at our referral center between 2014 and 2022 were reviewed. Patients with follow-up less than 3 months or in whom no clear description of initiated therapy could be identified by retrospective chart review, were excluded for evaluation of long-term outcomes. Clinical remission was defined according to the Hjortswang criteria as <3 stools/day or <1 watery stool/day. Data on relapse rates, subsequent therapies and surgery were collected.
Results: Three-hundred twenty-four patients were included, of whom 198 (CC 38.3%, LC 61.7%) were eligible for long-term assessment (Table 1) with a median follow-up of 3.7 [1.1-6.3] years. Median age at diagnosis was 63.4 [51.6-74.7] years. Concomitant diseases occurring in 3% or more included thyroid dysfunction (11.6%), coeliac disease (3.5%) and Parkinson's disease (5.1%), which numerically was more prevalent in the LC (7.4%) than CC (1.3%) population (p=0.09). A minority of patients had a family predisposition of IBD (5.6%). Spontaneous clinical remission occurred in 37 (18.6%) patients, while 4 (2.0%) patients were treated with 5ASA. Most patients (79.3%) were treated with corticosteroids, resulting in 81.1% clinical remission within 3 months. Eighty-six patients (54.8%) flared upon steroid tapering and/or withdrawal requiring corticotherapy reinitiation, prolongation or dose intensification. Due to steroid resistance or dependency, subsequent treatment options included 5ASA (n=14), cholestyramine (n=11), MTX (n=6) and azathioprine (n=8), all with limited effect. More advanced therapies are being used, including anti-TNF agents (n=25), vedolizumab (n=9) and JAK inhibitors (n=8). Eighteen patients (9.2%) are currently on maintenance advanced therapies for MC. Two treatment-refractory patients underwent colectomy.
Conclusions: In this large single-center retrospective analysis, steroids confirmed their first line position to induce clinical remission in MC. However, more than 50% of patients relapsed upon steroid tapering and/or withdrawal,

resulting in a substantial need for advanced therapy in this patient population. The long-term efficacy and safety of these advanced IBD therapies in MC should therefore be further investigated.

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PROMISING EFFICACY OF BIOLOGICALS AND SMALL MOLECULES FOR MICROSCOPIC COLITIS: RESULTS FROM A LARGE REAL-LIFE MULTICENTER COHORT. B. Verstockt (1), T. Taelman (1), S. Vavricka (2), Y. Zabana (3), M. Lenfant (1), G. Maicagne (4), M. Maillard (5), E. Savarino (6), N. Teich (7), V. Kiudelis (8), J. de la Revilla Negro (9), D. Ribaldone (10), M. Barreiro-de Acosta (11), S. Wildt (12), P. Rivière (13), M. Fumery (14), M. Truyens (15), A. Amiot (16), J. Marsal (17), A. Levartovsky (18), S. Vieujean (19), M. Somers (20), A. Cremer (21), I. Lutakov (22), N. Cohen (23), S. Dewit (24), L. Bajer (25), J. Rahier (26), A. Backman (27), S. Nancey (28), T. Choden (29), J. Van Dongen (30), A. Münch (31), M. Julsgaard (32) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] University Hospital Zürich, Zürich, Switzerland, Department of Gastroenterology and Hepatology, [3] Hospital Universitari Mútua Terrassa and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), , Spain, Department of Gastroenterology, [4] Centre Hospitalier de Marne-la-Vallee, Jossigny, France, Hepatogastroenterology Unit, [5] Lausanne Digestive Disease Center, Lausanne, Switzerland, Lausanne Digestive Disease Center, [6] University of Padua, Padua, Italy, Department of Surgery, Oncology and Gastroenterology, [7] Internistische Gemeinschaftspraxis, Leipzig, Germany, Gastroenterology, [8] Hospital of Lithuanian University of Health Sciences, Kaunas, Lithuania, Department of Gastroenterology, [9] Addenbrookes Hospital, Cambridge, United Kingdom, Department of Gastroenterology, [10] University of Turin, , Italy, Department of Medical Sciences, [11] University Hospital Santiago De Compostela CHUS, Santiago De Compostela, Spain, Department of Gastroenterology- IBD Unit, [12] Hvidovre Hospital, University Hospital of Copenhagen, Copenhagen, Denmark, Gastrounit, [13] CHU Bordeaux, France, Service d'hépato-Gastro-Entérologie et oncologie digestive, [14] University Hospital of Amiens, France, Department of gastroenterology, [15] University Hospital of Ghent, Belgium, Department of Gastroenterology, [16] Bicetre university hospital, Paris Saclay university, le Kremlin Bicêtre, France, Department of gastroentérology, [17] Skåne University Hospital, Sweden, Department of Gastroenterology, [18] Sheba Medical Center, Tel Aviv, Israel, Department of Gastroenterology, [19] University Hospital CHU of Liège, Belgium, Hepato-Gastroenterology and Digestive Oncology, [20] Antwerp University Hospital, Edegem, Belgium, Department of Gastroenterology and Hepatology, [21] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Gastroenterology and Hepatology, [22] University Hospital "Queen Joanna-ISUL" Sofia, Sofia, Bulgaria, Clinical Center of Gastroenterology, [23] Tel Aviv Medical Center, Tel Aviv, Israel, IBD Center, Department of Gastroenterology and Liver Diseases, [24] Noorderhart Mariaziekenhuis, Pelt, Belgium, Department of Gastroenterology, [25] Institute for Clinical and Experimental Medicine, Prague, Czech Republic, Department of Gastroenterology and Hepatology, [26] Université catholique de Louvain, CHU UCL Namur, Yvoir, Belgium, Department of Gastroenterology and Hepatology, [27] Ersta Hospital, Stockholm, Sweden, Department of Internal Medicine, [28] Lyon-Sud hospital, Hospices Civils de Lyon, Lyon, France, Department of Gastroenterology, [29] University of Chicago Medicine, Chicago, United States, Inflammatory Bowel Disease Center, [30] AZ Sint Maarten, Mechelen, Belgium, Department of Gastroenterology, [31] Linköping University, Linköping, Sweden, Department of Gastroenterology and Hepatology, [32] Aarhus University Hospital, Aarhus, Denmark, Aarhus, Denmark, Department of Hepatology and Gastroenterology.

Introduction: Microscopic colitis (MC) is a chronic inflammatory condition of the colon, resulting in an impaired quality of life due to debilitating watery diarrhea. First-line therapy consists of budesonide, though a subset of patients is refractory or becomes budesonide- dependent. Evidence for the efficacy of biologicals or small molecules in MC is sparse and limited to small case series.
Aim: We aimed to generate more real-life data on the efficacy of advanced therapies in the treatment of MC.
Methods: This retrospective series was collected as part of the CONFER project by ECCO and supported by the European Microscopic Colitis Group (EMCG). Cases of MC patients treated with advanced therapies were included through a standardised collection form. Clinical response was defined as a 50% reduction in stool frequency (SF); clinical remission was defined according to the Hjortswang criteria as < 3 stools/day or < 1 watery stool/day.
Results: Ninety-nine patients were identified, of whom all but one were previously treated with budesonide. Reasons for budesonide discontinuation included primary non-response (PNR, 16.3%), refractory disease (34.7%), budesonide dependency (38.8%), or adverse events (AE, 10.2%). In total, 165 treatment cycles with advanced therapy (47 IFX, 40 ADA, 47 VDZ, 10 UST, 14 JAK inhibitors, 7 other) were reported. First-line advanced therapies included mainly anti-TNF (76.8%) and VDZ (20.2%). Patients were exposed to anti-TNF therapy for a median of 1.4 [0.5-3.1] years, with a significant drop in SF after induction ($p<0.001$), resulting in 50.0% clinical remission. However, 63.0% ultimately discontinued anti-TNF therapy, mainly due to PNR (37.9%), loss-of-response (LOR, 36.2%) or AE (20.7%). VDZ induced 46.8% clinical remission, reflected in a significant drop in SF ($p<0.001$). Though, a 59.6% discontinuation rate was observed after a median 0.6 [0.3-1.3] years, mainly due to PNR (63.0%) and LOR (22.2%). Similarly, for UST a 40.0% clinical remission rate was accompanied by 60.0% therapy withdrawal, primarily due to PNR (83.3%).

In contrast, JAK inhibition resulted in 78.6% clinical remission, with a substantial drop in SF (p=0.002) and 21.4% discontinuation rate after a median exposure of 0.6 [0.3-1.6] years.
Conclusions: Almost all advanced therapies are used in budesonide refractory or dependent MC, with anti-TNF agents the most often used first-line options. However, anti-TNF discontinuation is frequent due to lack/loss of efficacy. VDZ and UST could be alternatives, but also have a substantial discontinuation rate. In this retrospective series, the small number (n=14) of JAK inhibitor treated patients had the highest remission rate, suggesting further research on the role of JAK inhibitors in MC.

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3D BIOPRINTING OF GELATIN DERIVATIVES: TOWARDS NOVEL SMALL INTESTINAL IN VITRO MODELS. L. Maes (1), A. Szabó (2), J. Van Haevermaete (2), I. Geurs (2), K. Dewettinck (3), S. Van Vlierberghe (2), D. Laukens (1) / [1] Ghent University, Ghent, Belgium, Department of Internal Medicine and Pediatrics, [2] Ghent University, Ghent, Belgium, Department of Organic and Macromolecular Chemistry, [3] Ghent University, Ghent, Belgium, Department of Food Technology, Safety and Health.

Introduction: Despite significant progress achieved in the field of inflammatory bowel disease (IBD) research, the precise cause of the disease has yet to be elucidated. Intestinal in vitro models can provide a fast and inexpensive alternative for in vivo studies. Nonetheless, many in vitro models lack the crypt or crypt-villus architecture as seen in the large and small intestine respectively and therefore fail to mimic the complexity of the gut.
Aim: In this study, we aim to improve the physiology of small intestinal in vitro models by the development of constructs that mirror the villi and crypts of the digestive tract, and exhibit physiological stiffness (± G'=1.52 kPa). For this purpose, we used gelatin-based photo-crosslinkable hydrogels, which have previously been demonstrated to be suitable candidates.
Methods: This study focused on the development of gelatin-methacryloyl-aminoethyl-methacrylate (gel-MA-AEMA)-, and gelatin-methacryloyl-norbornene (gel-MA-NB)-based biomaterial inks to fabricate 3D constructs, mimicking villi or a combination of villi and crypts, with digital light processing. The constructs were mechanically and morphologically evaluated with parallel plate rheology and cryo-scanning electron microscopy respectively. To assess the biocompatibility of the 3D constructs, a Caco-2/HT29-MTX co-culture in a 9:1 ratio was maintained for 21 days and confluency was confirmed with immunofluorescence. Gene expression, transepithelial electrical resistance (TEER) and paracellular permeability of the cells cultured on the constructs were compared to cells cultured on flat gel-MA-AEMA and gel-MA-NB hydrogels, a collagen type I coating or uncoated tissue culture plastic.
Results: Both gel-MA-AEMA and gel-MA-NB hydrogels exhibited physiologically relevant stiffness (1.9 ± 0.63 kPa and 1.64 ± 0.63 kPa respectively), but only the gel-MA-AEMA based biomaterial ink could be successfully utilized for printing constructs with villi and crypts. On all construct designs, confluency was reached and paracellular permeability of small sized marker molecules in combination with TEER measurements suggested the formation of a functional barrier over time, which was further confirmed by immunofluorescence and increased gene expression of tight junction proteins, occludin and ZO-1. The gene expression of enterocyte differentiation markers, villin-1, sucrase isomaltase and alkaline phosphatase, suggested the superior differentiation of Caco-2 cells on the 'only villi' and 'villi and crypts' constructs compared to flat hydrogels, collagen type I coating or uncoated tissue culture plastic
Conclusions: Although both hydrogels promoted functional barrier formation and enterocyte differentiation, gel-MA-AEMA was more suited for DLP than gel-MA-NB. In addition, culturing intestinal epithelial cells on the 3D villi-like constructs ameliorated cell differentiation compared to conventional 2D setups.

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FOOD ADDITIVES ON THE MUCOSAL BARRIER STUDY (FOAM): EFFECT OF DIETARY EMULSIFIERS ON INFLAMMATION, PERMEABILITY, AND THE MICROBIOME: PRELIMINARY RESULTS. J. Wellens (1), J. Vanderstappen (1), S. Hoekx (1), E. Vissers (2), M. Luppens (2), J. Raes (3), B. Verstockt (1), M. Ferrante (1), K. Verbeke (2), C. Matthys (4), S. Vermeire (1), J. Sabino (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [2] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing - Translational Research Center for Gastrointestinal Disorders, [3] Rega Institute-KU Leuven, Leuven, Belgium, Microbiology- Immunology and Transplantation Department, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Endocrinology.

Introduction: Dietary emulsifiers are common food additives that are omnipresent in a Western diet. Many emulsifiers including carboxymethyl cellulose, carrageenan and polysorbate-80 have been associated with intestinal inflammation and derangement of the microbiota. Due to these associations, they are frequently excluded in new dietary therapeutic strategies in inflammatory bowel disease. However, human data are scarce and involve only a limited number of emulsifiers.
Aim: We aimed to investigate the effect of five different emulsifiers on systemic and intestinal inflammation, intestinal permeability, and the gut microbiome in healthy volunteers.

Methods: We recruited 60 healthy volunteers to a 7-week double-blind placebo controlled randomized trial. After 1 week of recording their habitual diet (baseline), participants followed an emulsifier-free diet for 6 weeks, starting at baseline. After 2 weeks, participants combined the emulsifier-free diet with three daily brownies that contained either 2.75 g carboxymethyl cellulose, 1.350 mg polysorbate-80, 380 mg carrageenan, 3.55 g soy lecithin, or 8.72 g native rice starch, or no additives (placebo) for a period of 4 weeks. Anthropometric measurements and bio samples were taken at baseline, week 2 and week 6. Blood samples were collected for routine tests, Lipopolysaccharide-binding ELISAs, and serum proteomics using the Olink Target 96 Inflammation and Cardiometabolic panels. Stool samples were collected for analysis of the microbiota (16S rRNA sequencing), short chain fatty acids (Gas Chromatography – Mass Spectrometry), and faecal calprotectin analysis. Urine samples were collected following the 2-hour lactulose mannitol ratio protocol to measure paracellular small intestinal permeability (using Gas Chromatography – Mass Spectrometry). Lipopolysaccharide-binding ELISAs are being performed to measure paracellular intestinal permeability.
Results: Of the 60 healthy volunteers, two were excluded due to the use of non-steroidal anti-inflammatory drugs during the trial. Median (IQR) age was 25.5 years (23.0-33.0), median BMI was 22.7 kg/m^2 (21.2-25.6) and 19.0% of participants were male. There was a median weight loss of 0.1 kg (p-value=7.6*10^-4, paired Wilcoxon, unadjusted p-value). At week 6 and week 2, faecal calprotectin decreased significantly compared to baseline (p-value = 4.69*10^-4, and p-value= 2.81*10^-4 respectively, paired Wilcoxon, unadjusted p-value). No significant increase in faecal calprotectin was noted after consumption of any emulsifier during the trial. In the placebo arm, faecal acetic acid concentration was increased at week 2 (p=0.04). Compared to baseline, there was an increase in both acetic acid and propionic acid concentration (p-value =0.006 and p-value =0.04 respectively, paired Wilcoxon, unadjusted p-values) in the same arm at week 6.
Conclusions: In this double-blind placebo controlled randomized trial faecal acetic and propionic acid increased in the placebo arm, but did not after consumption of any of the emulsifiers. Faecal calprotectin did not increase after consumption of any emulsifier. Pending analysis will shed light on the effect of an emulsifier-free diet and distinct emulsifiers on the serum proteome, intestinal permeability and gut microbial changes.

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AN EMULSIFIER-FREE DIET IS ACCEPTABLE, FEASIBLE AND CAN BE ADHERED TO BY HEALTHY VOLUNTEERS. J. Wellens (1), M. Luppens (2), S. Hoekx (3), J. Vanderstappen (3), L. Van Elst (2), E. Vissers (2), M. Ferrante (3), B. Verstockt (3), K. Verbeke (2), C. Matthys (4), S. Vermeire (3), J. Sabino (3) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing - Translational Research Center for Gastrointestinal Disorders, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Endocrinology.

Introduction: Emulsifiers are associated with intestinal inflammation and therefore excluded in new dietary strategies in inflammatory bowel diseases (IBD).
Aim: We aimed to investigate the feasibility, acceptability, and adherence of an emulsifier-free diet in healthy subjects as part of the FOod Additives on the Mucosal barrier (FOAM) study.
Methods: We recruited 60 healthy volunteers to a 7-week interventional trial. After 1 week of recording their habitual diet (baseline), participants followed an emulsifier-free diet for 6 weeks. Participants were instructed on how to follow an emulsifier-free diet, yet were not advised on reducing UPF intake. Every 2 weeks after starting the emulsifier-free diet (week 2, 4, and 6), participants were asked about their experience on a 12-item questionnaire, including 5-point Likert scales, open-ended and multiple answer-type questions. Detailed food logs were kept in the smartphone application 'Fatsecret', including photographs to capture and record brand names as well. Manual calculation of all days with plausible energy intakes (800-4200 kcals per day for men and 600-3500 kcals for women) for at least 79.5% of the time was performed to exclude incomplete reporting. Emulsifier intake was measured as the number of servings of emulsifier-containing foods. Adherence rate was calculated as a percentage of mistake-free days.
Results: Of the 60 healthy volunteers, 2 were excluded due to NSAID use. Median (IQR) age was 25.5 years (23.0-33.0), median BMI was 22.7 kg/m2 (21.2-25.6) and 19.0% were male. Median percentage of plausible dietary logs was 100% (98.0-100%), and one participant was excluded due to inadequate reporting of the food logs. During the emulsifier-free diet, emulsifier intake significantly decreased (baseline vs. week 1; p=2.3x10-9, vs week 6; p=5.3x10-9, Friedman test with post-hoc Paired Wilcoxon), as well as UPF consumption according to the NOVA classification (baseline vs week 1; p=5.6x10-7, vs week 6; p=1.6x10-7, Friedman test with post-hoc Paired Wilcoxon). The adherence rate to the emulsifier-free diet was very high (median 88.1%, 76.2-95.2%). The median number of mistakes during the EFD was 6 (2-14), for a median number of 3 selected food items (1-5). Most mistakes were made in the categories of dairy-like products, meat products, and bakery goods. The top 3 reported challenges included restricted food choices, checking food labels, and longer shopping times. At week 6, For 70.7% the emulsifier-free diet was tasty to very tasty and for 72.4% it was acceptable to very acceptable on a five-point Likert scale. Hot meals and snacks were the most challenging meal types.
Conclusions: In this 7-week interventional trial in 60 healthy volunteers, adhering to an emulsifier-free diet was feasible and acceptable. While following the emulsifier-free diet, an inadvertent and stable decrease in UPF intake was noted. These finding represent important considerations when designing future dietary trials in IBD.

LIPOPOLYSACCHARIDE-BINDING PROTEIN (LBP) IN CROHN'S DISEASE (CD) PATIENTS: A PROMISING NON-INVASIVE BIOMARKER MONITORING DISEASE ACTIVITY. L. Toris (1), C. Minsart (2), C. Husson (1), D. Franchimont (2), C. Liefferinckx (2) / [1] ULB, Brussels, Belgium, Laboratory of Experimental Gastroenterology, [2] Hopitaux Universitaires de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Belgium, Dept. Gastroenterology, Hepato-Pancreatology and Digestive Oncology.

Introduction: Current biomarkers of inflammatory bowel disease (IBD) monitoring (serum C-reactive protein (CRP) and faecal calprotectin (FC)) have limitations in terms of specificity (SP) and sensitivity (SE), especially for Crohn's disease (CD) patients. Lipopolysaccharide-binding protein (LBP) is a soluble acute-phase protein and is thought to partly reflect intestinal permeability by binding to bacterial lipopolysaccharides. The search for new biomarkers to monitor disease activity would improve the management of IBD patients.
Aim: Our aim was to evaluate the potential of serum LBP in monitoring IBD.
Methods: This is a retrospective study including 69 IBD patients (43 CD and 26 ulcerative colitis (UC)) and 21 healthy controls (HC). Serum LBP levels were measured by enzyme-linked immunosorbent assay. Clinical, biological and endoscopic parameters were analysed for IBD patients. Statistical tests, including nonparametric tests and receiver operating characteristic (ROC) curve analysis, were used to evaluate the diagnostic accuracy of LBP.
Results: Participants had a median age of 29 [IQR 24.3-40] for HC and 32 [IQR 25-41] for IBD patients and 61.9% and 50.7% were female, respectively. The median BMI for HC was 22.6 [IQR 20-24.3] similar to IBDs with 21.9 [IQR 20.1-23.3]. According to Montreal classification, CD patients were classified in terms of age (A1=27.9%, A2=67.4% and A3=4.7%), behaviour (B1=55.8%, B2=27.9% and B3=16.3%) and location (L1=18.6%, L2=16.3% and L3=65.1%) and UC on the disease extent (E1=11.5%, E2=46.2% and E3=42.3%). Disease activity was assessed through CRP (5 mg/mL, [IQR 1.3-16] in CD vs 2.3, [IQR 1-15] in UC) and FC (600 µg/g, [IQR 460-800] in CD vs 600, [IQR 500-820] in UC) levels; supported by endoscopic reports (Quiescent, n=10 vs Active, n=33 in CD; and Quiescent, n=6 vs Active, n=20 in UC). Half of the IBD cohort (52.2%) was treated by biologics and 23.2% by immunosuppressors. In addition, at the moment of LBP measurement, 30% of patients used topical or systemic steroids. IBD patients displayed a significantly higher LBP median (29.6 µg/mL [IQR 19.8-38.8] in CD and 22.8 [IQR 13.7-38.8] in UC) than HC (5.5 [IQR 4.4-6.5], $P < 0.001$) with no overlapping distributions, a finding supported by an AUC of 0.997 and 0.989, respectively for CD and UC patients. In UC patients, LBP levels were not affected by disease endoscopic location and activity. On the contrary, in CD patients, LBP levels gradually increased with endoscopic severity, demonstrating a 1.7-fold rise in active patients compared to remitter patients ($P = 0.02$). LBP levels were higher in Montreal B1 compared to B2 and B3 CD patients ($P < 0.001$). Overall, a robust correlation was observed between LBP and CRP ($\rho=0.75$, $P < 0.001$). The correlation increased upon the exclusion of cases with normal CRP levels but active endoscopic disease ($\rho = 0.79$, $P < 0.001$). In those endoscopically active patients with normal CRP, LBP level was higher than in remitter patients (34.3 [IQR 29.4-37.6] vs 19.1, [IQR 10-24.7], $P = 0.01$) with a discriminative cut-off of 25 µg/mL, sensitivity was 100%, specificity 89%. LBP level also exhibited a positive correlation with FC ($\rho = 0.42$, $P < 0.01$). Similarly, this correlation was further strengthened after excluding cases where FC measurements did not align with endoscopic activity ($\rho = 0.53$, $P < 0.01$). It is noteworthy that most of those endoscopically active patients with normal FC had previously undergone ileocaecal resection. The median LBP for this new subgroup was 25.6 [IQR 18.5-31.5], reflecting again the interest of LBP measurement to accurately evaluate CD activity when FC lacks sensibility.
Conclusions: Our study suggests that LBP might be a promising non-invasive biomarker for monitoring disease activity, especially in CD patients. Furthermore, in clinical situations where current biomarkers (CRP and FC) lack sensitivity for assessing disease activity, LBP could be discriminative and help filling the gap for reliable therapeutic decisions.

VARIETY BEACH STUDY: REAL-WORLD TREATMENT PATTERNS FOR VEDOLIZUMAB INTRAVENOUS AND SUBCUTANEOUS MAINTENANCE DOSING OBSERVED OVER 1 YEAR IN STUDIES FROM BELGIUM, AUSTRIA AND SWITZERLAND. E. Louis (1), G. Novacek (2), P. Hrúz (3), C. Högenauer (4), S. Vavricka (5), A. Moschen (6), L. Biedermann (7), C. Mächler (8), B. Stemberger (9), G. Van Gassen (10), F. Baert (11) / [1] CHU de Liège, Liège, Belgium, Gastro-enterologie, [2] Medical University of Vienna, Vienna, Austria, Internal Medicine, [3] Clarunis Universitäres Bauchzentrum, Basel, Switzerland, Gastro-enterology, [4] Medical University Graz, Graz, Austria, Gastro-enterology, [5] University Hospital Zürich, Zürich, Switzerland, Gastro-enterology and hepatology, [6] Johannes Kepler University, Linz, Austria, Internal Medicine, [7] University Hospital, Zurich, Switzerland, Gastro-enterology and hepatology, [8] Takeda Pharma AG, Glattpark, Switzerland, Medical Affairs, [9] Takeda Ges.m.b.H,, Wien, Austria, Medical Affairs, [10] Takeda Belgium, Brussels, Belgium, Medical Affairs, [11] AZ Delta, Roeselare, Belgium, Gastroenterology.

Background: Vedolizumab (VDZ) is approved for moderate to severe ulcerative colitis (UC) and Crohn's disease (CD) as intravenous (IV) or subcutaneous (SC) formulations. Real-world data on VDZ treatment patterns in patients (pts) with inflammatory bowel disease (IBD) comparing VDZ IV or SC maintenance are still scare.

Aim: Evaluate real-world data on VDZ treatment patterns in patients with IBD on either VDZ IV or SC maintenance therapy.
Methods: Methods: Three prospective, non-interventional, observational studies following an umbrella protocol enrolled pts in Belgium (NCT04959851), Austria (NCT04890262) and Switzerland (NCT04989907) from Aug 2021 to Jun 2022. Adults initiating VDZ IV induction per the product label or continuing VDZ IV maintenance with the option to switch to SC administration, were eligible. The primary endpoint was VDZ treatment persistence at 1 year. Administration route, dosing frequency, reasons for regimen change and safety endpoints were also assessed. Non- responder imputation was applied for pts discontinuing treatment, discontinuing the study or lost to follow-up. A descriptive analysis was performed.
Results: Results: Of 377 pts enrolled, 373 (UC=218, CD=155) were included in this interim analysis. At enrolment, 287 (77%) (UC=159, CD=128) already received VDZ IV maintenance for median 2.8 (0–12.6) years and 86 (23%) (UC=59, CD=27) were to start VDZ induction (baseline pt characteristics summarized in Table 1). For pts enrolled on VDZ IV maintenance, 12 discontinued vedolizumab, 34 discontinued the study and 14 were lost to follow-up; resulting in a VDZ persistence rate at 1 year of 79% (227/287). Of pts in this cohort persistent on VDZ at 1 year (n=227; UC=124, CD=103), 39% (88/227) switched from VDZ IV maintenance to SC during the study. For pts initiating VDZ induction, 10 discontinued VDZ,16 discontinued the study and 3 were lost to follow-up; resulting in a VDZ treatment persistence of 66% (57/86). Of pts from this cohort persistent on VDZ at 1 year (n=57; UC=43, CD=14), 56% (32/57) switched to VDZ SC during the study (Figure 1). Overall, the most common reasons for administration route changes were pt decision 98/161 (61%; UC=56%, CD=67%), end of induction (planned switch: 10%; UC=14%, CD=5%) and disease adequately controlled (6%; UC=7%, CD=3%). Adverse events (AEs) occurred in 48 pts (13%) (UC=20, CD=28) and serious AEs in 6 pts (2%) (UC=3: Budd-Chiari syndrome, death cause unknown, UC worsening; CD=3: bronchopneumonia, gastroenteritis, recurrent urinary tract infection).
Conclusions: Conclusion: Real-world data from prospective observational studies in Belgium, Austria and Switzerland reported high persistence of VDZ IV and SC maintenance treatment over 1 year. Decisions on route of administration change were most frequently driven by patients. Safety results were consistent with the known safety profile of VDZ.

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REDUCED PARENTERAL SUPPORT NEEDS WITH THE NOVEL LONG-ACTING GLP-2 ANALOG APRAGLUTIDE IN PATIENTS WITH SHORT BOWEL SYNDROME WITH INTESTINAL FAILURE AND COLON IN CONTINUITY AT 52 WEEKS. A. Verbiest (1), M. Krogh Hvistendahl (2), F. Bolognani (3), C. Li (3), N. N. Youssef (4), P. Bekker Jeppesen (2), F. Joly (5), T. Vanuytsel (1) / [1] KUL - University of Leuven, Leuven, Belgium, Translational Research Center for Gastrointestinal Disorders (TARGID), [2] Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark, Department of Intestinal Failure and Liver Diseases, [3] VectivBio, Basel, Switzerland, Clinical Development, [4] VectivBio, Basel, Switzerland, Medical Affairs, [5] Hopital Beaujon (AP-HP), France, Centre for Intestinal Failure, Department of Gastroenterology and Nutritional Support.

Introduction: Short bowel syndrome (SBS) is a rare gastrointestinal condition caused by extensive surgery, e.g. following inflammatory bowel disease or mesenteric ischemia; or congenital disease, leaving a small intestine of less than 200 cm. Patients with SBS are at high risk to develop intestinal failure (SBS-IF) requiring parenteral support (PS). Glucagon-like peptide-2 (GLP-2) analogs stimulate adaptation of the remaining gut resulting in increased intestinal absorption and reduced PS needs. Extensive literature is available on the effect of teduglutide in patients without a remaining colon. However, in SBS-IF with a colon-in-continuity (CiC), where there is less dependency on IV fluid compared to calories, the impact of GLP-2 analogs is much less established. Apraglutide (APRA) is a novel, long-acting GLP-2 analog in development for SBS-IF.
Aim: This multicenter, open-label, phase 2 study in SBS-IF-CiC aims to investigate the safety and efficacy of APRA in reducing PS needs at 52 weeks.
Methods: STARS Nutrition is a 52-week study in adult patients with SBS-IF-CiC receiving once-weekly subcutaneous APRA injections (5 mg). Metabolic balance studies were performed at baseline and 4 weeks with stable PS, followed by a 48-week PS adjustment period. During monthly 48h fluid balance assessments, oral fluid intake was kept constant by adhering to an individual predefined drinking menu while urine was collected. PS was reduced according to a predefined algorithm if an increase in mean daily urinary output of ≥10% was observed. Safety was the primary endpoint. Secondary endpoints included changes in weekly PS volume, energy content, and PS days, and proportion of clinical responders (PS reduction of ≥20%). Data are presented as mean (95% CI) unless specified otherwise. Nominal p-values are calculated using paired T-tests with significance set at 0.05.
Results: Nine patients were included and comprise the full study population. Small bowel length was 19 (range 0-50) cm and 79 (range 43-100) % of the colon was in continuity. Patients had baseline PS needs of 10 (range 4-21) L distributed over 5.2 (range 3 – 7) days/wk. APRA had an acceptable safety profile, consistent with previous data. All patients experienced ≥1 adverse event (AE) after initiating APRA; a total of 127 AEs was reported. Three patients experienced serious AEs. APRA was interrupted for 1 week in one patient with acute cholangitis; APRA was restarted and successfully continued to study completion. Absolute weekly PS volume decreased significantly by -4702 (-6539

– -2865) mL/wk (p=0.0004). Accordingly, PS energy content significantly decreased by -3510 (-4991 – -2029) kcal/wk (p=0.0006). All patients qualified as clinical responders. Seven patients (78%) achieved ≥1 day off PS of whom two patients (22%) reached enteral autonomy. Patients gained an additional 2.1 (0.7 – 3.6) days off per wk. Body weight and daily urine output remained constant despite PS reductions.
Conclusions: STARS Nutrition prospectively shows evidence for clinical benefit of a long-acting GLP-2 analog in SBS-IF-CiC. APRA has an acceptable safety profile and significantly reduces PS needs in patients with SBS-IF-CiC resulting in days without PS.

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STRIDE-II RECOMMENDATIONS IN ROUTINE IBD PATIENT MANAGEMENT: A NESTED STUDY OF THE BELGIAN POPULATION WITHIN THE REAL-WORLD INTERNATIONAL MULTICENTRE IBD-PODCAST STUDY. B. Verstockt (1), J. Schrevens (2), A. Colard (3), F. D'Heygere (4), B. Strubbe (5), J. Van Dongen (6), C. Leitner (7), B. Gillon (2), L. Ghys (2), D. Franchimont (8) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and hepatology, [2] Abbvie, Wavre, Belgium, Medical Affairs, [3] Clinique Mont Legia - CHC Groupe Santé, Liège, Belgium, Gastroenterology, [4] AZ Groeninge, Kortrijk, Belgium, Internal Medicine/Gastroenterology, [5] AZ Sint-Lucas, Ghent, Belgium, Gastroenterology and hepatology, [6] AZ Sint Maarten, Mechelen, Belgium, Gastroenterology, [7] AbbVie Switzerland, Cham, Switzerland, Medical Affairs, [8] Hopital Erasme, ULB, Belgium, Gastroenterology.

Introduction: Suboptimal disease control (SDC) in inflammatory bowel disease (IBD) results in disease progression and negative long-term outcomes. Disease monitoring tools have been developed in addition to disease management recommendations, endorsing a treat-to-target approach. The recently updated Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE-II) recommendations not only include biomarkers and endoscopy, but also clinical, and patient reported outcomes (PROs) to guide treatment decisions and monitor treatment response.
Aim: The objective was to evaluate the real-world IBD patient management according to STRIDE-II recommendations in the Belgian population within the multicenter IBD-PODCAST study.
Methods: IBD-PODCAST was an international, cross-sectional, real-world study conducted in 103 sites in ten countries between November 2022 and January 2023. Here we present data from the six Belgian participating centers. Analysis included patient- and physician-reported measures, and retrospectively assessed components of the last 12 months. Pre-defined indicators ('red flags') suggesting SDC according to the STRIDE-II recommendations included clinical parameters, biomarkers, endoscopy, other imaging and patient questionnaires such as the Short Inflammatory Bowel Disease Questionnaire (SIBDQ).
Results: A total of 132 consecutive patients (CD: n=75; UC: n=57), with a mean (standard deviation [SD]) age of 43.2 [14.2] years (range: 19-80) and mean [SD] disease duration of 14.2 [10.2] years, were enrolled. According to STRIDE-II, in CD, the majority (78.7%) of patients were in long-term (LT) treatment, while 8.0% were in intermediate and 13.3% were in short-term. For UC, most patients (84.2%) were in LT treatment, with 3.5% in intermediate and 12.3% in short-term. Among CD and UC patients, 97.3% and 94.7% were on targeted immunomodulators (TIM) respectively, of which 45.2% and 44.4% were first-time TIM users. In CD, 88.4% received biologicals, 7.8% immunomodulators, and 3.9% steroids. In UC, 68.1% received biologicals, 19.4% oral 5-aminosalicylic acid (ASA), 5.6% Janus kinase inhibitor (JAK-I), 4.2% immunomodulators, and 2.8% steroids. 'Red flags' were reported in 46.7% (n=35) of CD and 42.1% (n=24) of UC patients. In CD patients, impaired QoL (SIBDQ <50) was identified as the most common 'red flag' (n=26, 74.3%), followed by clinically significant extra-intestinal manifestations (EIMs; n=9, 25.7%) and presence of active fistula/perianal disease (n=6, 17.1%). In UC patients, steroid overuse (defined as prolonged (>6 weeks) administration of prednisolone ≥10 mg/dL (or equivalent) or >1 steroid course under the current therapy within the previous 12 months) was the most common 'red flag' (n=14, 58.3%), followed by impaired QoL (n=11, 45.8%) and failure to achieve endoscopic remission (n=8, 33.3%). Failure to achieve clinical improvement (>50% reduction of symptoms since therapy initiation) was similarly present across both diseases (16.7% for UC, 17.1% for CD). Interestingly, in both LT CD (n = 33) and LT UC patients (n=20) with SDC, 30% presented with two or more 'red flags'. Among the group of patients with impaired QoL in the LT CD (n=24) and UC window (n=8), 38% and 63% respectively also exhibited other 'red flags'.
Conclusions: This study provides a snapshot of the routine IBD management in the Belgian cohort of the real-world global multicentre IBD-PODCAST study according to the STRIDE-II recommendations. This study highlights that a significant proportion of the Belgian patients may have SDC in both CD and UC, of which the most significant 'red flag' was impaired QoL these patients. These results are in line with the German and Portuguese cohort of the IBD-PODCAST study. The data underscore the continued high disease burden among IBD patients in Belgium, highlighting the need for enhanced disease management strategies to further improve long-term outcomes. The limitations of the study include the lack of stratification according to patient therapeutic management subgroups: steroid use for first induction or relapse, biologics naïve/ previously exposed, biologics w/o response (i.e. loss of response), biologics escalation/ de-escalation, prior or post-surgery status, disease severity (stable or progressive disease), patient adherence/compliance, and patient access to health care.

CLINICAL PARAMETERS OF STRIDE-II LEADING TO ADJUSTMENT IN MONITORING OR THERAPY IN IBD PATIENTS – RESULTS FROM THE BELGIAN COHORT OF THE IBD-PODCAST STUDY. B. Verstockt (1), J. Schrevens (2), A. Colard (3), F. D'Heygere (4), B. Strubbe (5), J. Van Dongen (6), C. Leitner (7), J. Morrens (2), L. Ghys (2), D. Franchimont (8) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and hepatology, [2] Abbvie, Wavre, Belgium, Medical Affairs, [3] Clinique Mont Legia - CHC Groupe Santé, Liège, Belgium, Gastroenterology , [4] AZ Groeninge, Kortrijk, Belgium, Internal Medicine/Gastroenterology, [5] AZ Sint-Lucas, Ghent, Belgium, Gastroenterology and hepatology, [6] AZ Sint Maarten, Mechelen, Belgium, Gastroenterology, [7] AbbVie Switzerland, Cham, Switzerland, Medical Affairs, [8] Hopital Erasme, ULB, Belgium, Gastroenterology.

Introduction: To guide physicians' treatment decisions in inflammatory bowel diseases (IBD), the last STRIDE-II recommendations defined specific target values to be achieved within specified timeframes. However, there is insufficient evidence on clinical decision-making in IBD based on STRDE-II and which clinical parameters trigger additional monitoring or treatment modification. IBD-PODCAST was an international cross-sectional real-world study with 6 Belgian centres. The study aimed to evaluate disease control per STRIDE-II and its impact on quality of life of patients with Crohn's disease (CD) or ulcerative colitis (UC).
Aim: This analysis focused on monitoring techniques and clinical parameters leading to physician action in the Belgian centres.
Methods: Clinically relevant parameters included: (i) excess steroid exposure (>6 weeks prednisolone ≥10 mg/dL (or equivalent)), (ii) lack of clinical improvement (CI) [<50% reduction in symptoms since therapy initiation (in CD based on stool frequency (SF)/abdominal pain (AP); and in UC based on liquid stools and rectal bleeding (RB))], (iii) faecal calprotectin (fCAL) >250µg/g, (iv) C-reactive protein (CRP) >0.5mg/dL, (v) anemia (Hb <11 g/dl for females, <12 g/dl for males), (vi) extra-intestinal manifestations, or (vii) MRE/IUS/endoscopy indicating active inflammation in the past 8 weeks. Additional parameters included >3 liquid stools/day and HBI>4 for CD; Mayo SF-subscore >0 and Mayo RB-subscore >0 for UC. Physician actions were defined as additional monitoring (diagnostic test, imaging) or treatment adjustment (change, intensification, or addition of medication).
Results: The Belgian cohort included 75 CD and 57 UC patients with a mean (standard deviation [SD]) age of 43.2 [14.2] years (range: 19-80) and disease duration of 14.2 [10.2] years. In CD, 88.4% received biologicals, 7.8% immunomodulators, and 3.9% steroids. In UC, 68.1% received biologics, 19.4% oral 5-aminosalicylic acid, 5.6% JAK-I, 4.2% immunomodulators, and 2.8% steroids. At the study visit, CRP (±2 weeks) was most monitored, in both CD (n=47; 62.7%) and UC (n=31, 54.4%) patients. FCAL (±2 weeks) was evaluated in 15 (20%) CD and 3 (5.3%) UC patients. Endoscopy (±8 weeks) was performed in 5 (6.7%) CD and 16 (28.1%) UC patients, with 7 (9.3%) CD patients receiving other imaging techniques. During the prior 12 months, imaging was performed in 37 (49.3%) CD and 33 (57.9%) UC patients. Endoscopy accounted for 81.1% and 93.9%, MRE/CT for 16.2% and 12.1%, and IUS for 18.9% and 3% of CD and UC patients, respectively. Any imaging within the past 12 months combined with biochemical assessment at the study visit (± 2 weeks) was performed in 61 (81.3%) CD and 45 (78.9%) UC patients. Conversely, 14 (18.7%) CD and 12 (21.1%) UC patients had not been monitored biochemically at the study visit or via imaging within the past 12 months. Of those, 7 (50%) CD and 5 (42%) UC patients had suboptimal disease control per STRIDE-II. At the study visit, 38 (50.7%) CD and 23 (40.4%) UC patients exhibited clinically relevant parameters, triggering physician actions in 17 (44.7%) CD and 13 (57%) UC patients. Conversely, no additional monitoring or treatment adjustments took place in 21 (55.5%) CD and 10 (43.5%) UC patients. Strongest triggers for treatment adjustment were lack of CI in CD and RB in UC, while lack of CI triggered additional monitoring most in both diseases.
Conclusions: Clinical decision-making in IBD is complex and not based on single parameters or a defined time frame. Absence of actions on STRIDE-II clinical parameters may be due to intentional clinical decision, patient adherence, patient access, or suboptimal patient management. However, the results highlight the need for monitoring strategies and prompt treatment actions to optimize disease control and enhance patient outcomes in IBD. Study limitations include lack of stratification according to patient therapeutic management subgroups: steroid use for first induction or relapse, biologics-naïve/experienced/loss-of-response, biologics escalation/de-escalation, prior or post-surgery status, stable/progressive disease, patient adherence/compliance, patient access to health care, and short time window for fCAL evaluation.

DISTINCT BLOOD PROTEIN PROFILES ASSOCIATED WITH ILEAL AND COLONIC ULCERS IN CROHN'S DISEASE. N. Pierre (1), V. Huynh-Thu (2), D. Baiwir (3), S. Vieujean (1), E. Bequet (1), C. Reenaers (4), C. Van Kemseke (4), C. Salée (1), C. Massot (1), M. Fléron (3), G. Mazzucchelli (5), L. Trzpiot (5), G. Eppe (5), E. De Pauw (5), E. Louis (1), M. Meuwis (1) / [1] University of Liege, Liege, Belgium, Laboratory of Translational Gastroenterology, GIGA-institute, [2] University of Liege, Liege, Belgium, Department of Electrical Engineering and Computer Science, [3] University of Liege, Liege, Belgium, GIGA Proteomics Facility, [4] Liege University Hospital, Liege, Belgium,

Hepato-Gastroenterology and Digestive Oncology Department, [5] University of Liege, Liege, Belgium, Laboratory of Mass Spectrometry, MolSys Research Unit.

Introduction: Ileal and colonic Crohn's disease (CD) are nowadays considered as separate entities. Studies are needed to better characterise the biological specificities of these subphenotypes. In fine, this research should offer opportunities for the development of personalised medicine.
Aim: We aim to: 1) characterise the blood protein profiles associated with ileal and colonic ulcers; 2) find blood biomarker candidates more specifically associated with ileal or colonic ulcers and comparing their performance to CRP.
Methods: By combining different technologies (proximity extension assay, selected reaction monitoring and high-sensitivity turbidimetric immunoassay (hsCRP)), 207 serum proteins were measured in CD patients presenting no endoscopic lesions (endoscopic remission) (n=23), isolated ileal ulcers (n=17) or isolated colonic ulcers (n=16). To compare the endoscopic activity between the ileum and colon, and in order to obtain an assessment of the overall lesion burden, we used the Crohn's disease endoscopic index (CDEIS) without dividing its total score (sum of each gut segment) by the number of inspected segments. This score was retrospectively calculated and called "total CDEIS". The Wilcoxon-Mann-Whitney test was used for the differential analyses (isolated ileal ulcers vs endoscopic remission; isolated colonic ulcers vs endoscopic remission). From this analysis, proteins showing a differential abundance were selected and their abundance values were re-scaled to be comprised between 0 and 1. Then, those proteins were systematically combined by two using the product or the sum of their re-scaled values (n=30 combinations for the detection of ileal ulcers; n=306 combinations for the detection of colonic ulcers). The classification performance (isolated ileal ulcers vs endoscopic remission; isolated colonic ulcers vs endoscopic remission) of individual markers or their combinations were given by the area under the receiver operating characteristics curve (AUROC). The AUROC values were statistically compared to a random classifier (AUROC=0.5) and the AUROC of CRP using the bootstrap test (2000 replications).
Results: The median of the total CDEIS was higher in CD patients with isolated colonic ulcers than those with isolated ileal ulcers (23.1 vs 8.0). When compared to endoscopic remission, the presence of isolated ileal ulcers and isolated colonic ulcers were specifically associated with the level of 6 and 18 serum proteins, respectively: (high level: JUN, CNTNAP2; low level: FCRL6, LTA, CLEC4A, NTF4); (high level: hsCRP, IL6, APCS, CFB, MBL2, IL7, IL17A, CCL19, CXCL10, CSF3, IL10, CLEC4G, MMP12, VEGFA; low level: CLEC3B, GSN, TNFSF12, TPSAB1). No protein was associated with both isolated ileal ulcers and isolated colonic ulcers. All CD patients in endoscopic remission showed a normal level of hsCRP (<5 mg/L). Compared to CD patients in endoscopic remission, CD patients with isolated colonic ulcers showed an increased median level of hsCRP (1.3 vs 5.9 mg/L, p-value=0.0045) and this was not the case for CD patients presenting isolated ileal ulcers (1.3 vs 2.2 mg/L, p-value=0.13). hsCRP detected ileal and colonic ulcers with an AUROC of 0.64 (p-value=0.07) and 0.77 (p-value=0.001), respectively. To discriminate ileal ulcers from endoscopic remission, 20 proteins showed an AUROC significantly different than 0.5 and numerically higher than hsCRP (0.65-0.75 vs 0.64, non-significant): FCRL6, LTA, JUN, CLEC4A, CNTNAP2, NTF4, ITGB6, ITM2A, TNFSF12, APCS, IL17C, SERPINA3, CLEC4G, MASP1, CD83, PIK3AP1, LY75, C8G, CFB, TREM1. To discriminate colonic ulcers from endoscopic remission, 2 proteins showed an AUROC significantly different than 0.5 and numerically higher than hsCRP: CSF3 (0.85 vs 0.77, non-significant), IL7 (0.79 vs 0.77, non-significant). To discriminate ileal ulcers from endoscopic remission (AUROC), CLEC4A × LTA was the best combination when compared with hsCRP (0.82 vs 0.64, p-value=0.057). To discriminate colonic ulcers from endoscopic remission (AUROC), hsCRP × CSF3 was the best combination when compared with hsCRP (0.85 vs 0.77, p-value=0.020).
Conclusions: In CD patients, ileal and colonic ulcers were associated with distinct systemic responses. hsCRP showed a better capacity to detect patients with colonic than ileal ulcers. Some markers might help to detect ileal ulcers or to improve the ability of CRP for detecting colonic ulcers.

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SAFETY AND EFFECTIVENESS OF VEDOLIZUMAB AND USTEKINUMAB IN INFLAMMATORY BOWEL DISEASE PATIENTS AFTER LIVER TRANSPLANTATION FOR PRIMARY SCLEROSING CHOLANGITIS: RESULTS FROM AN ECCO-CONFER CASE SERIES. T. Holvoet (1), E. Brusselle (2), B. Verstockt (3), M. Lenfant (3), M. Julsgaard (4), D. Drobne (5), A. Thakor (6), H. Gordon (7), T. Molnar (8), E. Savarino (9), D. Ribaldone (10), P. Miheller (11), S. Vieujean (12), I. Candel (13), L. Menchen (14), D. Bettenworth (15), P. Eder (16), A. Issachar (17), T. Lobaton (2) / [1] Vitaz, Sint-Niklaas, Belgium, Gastroenterology, [2] Ghent University Hospital, Ghent, Belgium, Gastroenterology, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [4] Aarhus University Hospital, Aarhus, Denmark, Aarhus, Denmark, Hepatology and Gastroenterology, [5] University Medical Centre Ljubiljana, Ljubiljana, Slovenia, Gastroenterology, [6] Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom, Gastroenterology, [7] Royal London Hospital, London, United Kingdom, Gastroenterology, [8] University of Szeged, Szeged, Hungary, Gastroenterology, [9] University of Padua, Padua, Italy, Gastroenterology, [10] University of Turin, Italy, Gastroenterology, [11] Semmelweis University, Budapest, Hungary, Gastroenterology, [12] CHU Liege, Liège, Belgium, Gastroenterology, [13] Udaondo`s Hospital, Buenos Aires, Argentina, Gastroenterology, [14] Hospital General Universitario "Gregorio Marañón, Madrid, Spain, Gastroenterology, [15] Münster University Hospital, Münster, Germany, Clinical Medicine, [16] Poznan University,

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Introduction: Primary sclerosing cholangitis (PSC) is a chronic progressive cholestatic liver disease often necessitating liver transplantation (LTX). Approximately 70% of PSC patients have a concomitant diagnosis of inflammatory bowel disease (IBD) and could need treatment with biological therapy on top of the immunosuppression to prevent transplant rejection. Vedolizumab (VDZ) and ustekinumab (UST), both agents with a favorable safety profile, are often used in this population despite lack of data concerning safety and effectiveness in the post-LTX setting.
Aim: To evaluate real-life effectiveness and safety of VDZ and UST in PSC-IBD patients who underwent a liver transplantation
Methods: A retrospective multicenter case series was performed as a part of the European Crohn's and Colitis Organisation [ECCO] Collaborative Network of Exceptionally Rare case reports [CONFER] project. Primary endpoints were clinical and endoscopic remission at week 52, occurrence of infectious complications, occurrence of malignancy, hospitalizations, occurence of extra-intestinal manifestations (EIM) and death after liver transplantation.
Results: In this retrospective study, 58 patients (male n= 34 (59%), median age 42 (interquartile range (IQR) 32-52) were included across 16 participating centers of which 24 (38%) were treated with UST and 40 (63%) with VDZ. Twelve patients (20%) were diagnosed with Crohn's disease (CD), 44 (76%) with ulcerative colitis (UC), 2 (3%)- with unclassified IBD (IBD-U) and in 12 (20%) patients had an ileal pouch anal anastomosis (IPAA). Median disease duration was 16 years (IQR 13-26) and 33 (56%) had received biological therapy prior to LTX (33% anti-TNF, 11% VDZ, 5% UST). Median disease duration for PSC was 15.5 years (IQR 11-25) and median time since LTX was 6 years (IQR 4-10). Clinical remission, assessed according to physician global assessment, at week 52 was achieved in 44% of VDZ compared to 38% of UST treated patients (p=0.17), while endoscopic remission was seen in 17% of patients in the VDZ group versus 33% in the UST treated patients (p=0.87). Clinical effectiveness was similar across CD (respectively 33% and 20%), UC (33% and 37%) and IPAA patients (36% vs 60%). Infectious complications occurred in 21 patients (29%; 27% VDZ vs 33% UST) post LTX on biological therapy (p=0.66), malignancy occurred in 10 patients (14.1%, 12.8% VDZ vs 16.7% UST, p=0.66), hospitalizations in 32 (45%; 51% VDZ vs 34% UST, p=0.15), and death in 2 patients (3.4%; 2.1% VDZ vs 4.2% UST, p=0.66).
Conclusions: In IBD-PSC patients who underwent LTX both UST and VDZ show similar effectiveness with clinical remission rates of respectively 44% and 38% after 1 year. Safety profiles are similar although infectious complications and occurrence of malignancy remains an important concern in this patient group.

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OUTCOMES IN PATIENTS STOPPING BIOLOGIC DURING THE FIRST TRIMESTER OF PREGNANCY: A RETROSPECTIVE MONOCENTRIC STUDY. L. Monin (1), C. Reenaers (1), S. Grandfils (2), P. Latour (1), C. Van Kemseke (1), S. Kropp (1), E. Louis (1), S. Vieujean (1) / [1] CHU Liege, Liège, Belgium, Hepato-Gastroenterology and Digestive Oncology, [2] CHU Liege, Liège, Belgium, Gynecology.

Introduction: Both the American Gastroenterological Association (AGA) and the European Crohn's and Colitis Organisation (ECCO) recommend to continue biologic during the whole pregnancy and until the third trimester, respectively. However, these positions are associated with a baby's exposure to the drug and from our clinical practice are not necessarily in line with patients' wishes and fears. In patients in full clinical and biologic remission, stopping biologic before it is actively transported through the placenta (around the week 20) would be a possible approach to get around these drawbacks.
Aim: We aimed to assess the outcome of disease activity and pregnancies in patients stopping biologic before the week 20.
Methods: We performed a retrospective monocentric study. All patients who gave birth between 2010 and 2023 were included. The following parameters were collected: clinical and demographic characteristics, biomarkers (CRP and faecal calprotectin before pregnancy and during the 3 trimesters), IBD treatment at time of pregnancy, whether it was stopped during pregnancy, when and in what circumstance (patient versus medical agreement). We also looked at the disease course, whether a relapse occurred (defined as the need to take corticosteroids, a biologic, or surgical resection), and the pregnancy outcome.
Results: A total of 185 pregnancies were reported in 143 patients (73.4% CD and 26.6% UC). Among these women, 106 (74.1%), 32 (22.4%) and 5 (3.5%) reported one, two or 3 or more pregnancies, respectively. The biologic was stopped before conception for 9 pregnancies and 90 pregnancies started under biologics (anti-TNF, vedolizumab or ustekinumab). Of these, biologic was continued until delivery in 10 (11.1%) patients, whereas it was stopped before the week 20 for the others (88.9%). Among patients who stopped biologics before conception, before the week 20, and those who continued biologics through delivery: 3/9 (33.3%), 13/80 (16.3%; including 10/66 or 15.2% among those stopping on medical agreement) and 4/10 (40%) relapsed, respectively. Among the 10 relapses in patients who stopped in first trimester on medical agreement, 6 had normal biomarkers before cessation (unknown for the others). Concerning the pregnancy's outcomes (caesarean, preterm birth, low birth weight ≤2500gr and perinatal death), for the different

treatment groups at time of pregnancy (no treatment (n=50); treatment with 5-ASA/immunosuppressor/corticosteroids (n=36); biologic stopped before pregnancy (n=9); biologic stopped before week 20 (n=80) and biologic throughout pregnancy (n=10)), we observed : 15/50 (30%), 13/36 (44.4%), 4/9 (44.4%), 31/80 (38.8%), 3/10 (30%) caesereans; 4/50 (8%), 5/36 (13.9%), 1/9 (11.1%), 16/80 (20%), 0/10 (0%) preterm births; 4/50 (8%), 1/36(2.8%), 0/9 (0%), 10/80 (12.5%), 0/10 (0%) low birth weights; 0/50 (0%), 1/36 (2.8%), 0/9 (0%), 1/80 (1.3%), 1/10 (10%) perinatal deaths, respectively.
Conclusions: Biologic discontinuation before week 20 on medical agreement was associated with relapse in 15.2% of cases. Fate of disease activity and pregnancies in patients stopping biologic before week 20 should be studied prospectively in a dedicated study.

- I28 -

NO DIFFERENCE IN PROGRESSION OF DISABILITY 2 YEARS AFTER STOPPING INFLIXIMAB OR IMMUNOSUPPRESSANT VS. CONTINUING COMBINATION THERAPY IN PATIENTS WITH CD IN SUSTAINED STEROID-FREE REMISSION: A SUBANALYSIS OF SPARE. S. Vieujean (1), K. Desseaux (2), D. Laharie (3), J. Satsangi (4), N. Ding (5), B. Siegmund (6), G. D'Haens (7), L. Picon (8), P. Bossuyt (9), L. Vuitton (10), P. Irving (11), S. Viennot (12), C. Lamb (13), R. Pollok (14), F. Baert (15), M. Nachury (16), M. Fumery (17), C. Gilletta (18), M. Resche-Rigon (19), Y. Bouhnik (20), J. Colombel (21), E. Hertervig (22), E. Louis (1) / [1] University Hospital CHU of Liège, , Belgium, Hepato-Gastroenterology and Digestive Oncology, [2] INSERM U717 Saint-Louis Hospital, , France, Department of statistics, [3] Hôpital Haut-Lévêque– Université de Bordeaux, , France, Service d'Hépato-Gastro-Entérologie et oncologie digestive CHU de Bordeaux, [4] John Radcliffe Hospital, United Kingdom, Translational Gastroenterology Unit, Nuffield Department of Medicine, [5] St Vincent's Hospital Melbourne, Australia, Department of Gastroenterology, [6] Universitätsmedizin Berlin, Germany, Medical Department, Division of Gastroenterology, Infectious Diseases and Rheumatology, Charité, [7] Amsterdam University Medical Centres, Netherlands, Department of Gastroenterology and Hepatology, [8] Hôpital Trousseau, France, Hépato-Gastro-Onco-Entérologie, [9] Imelda General Hospital, Belgium, Imelda GI Clinical Research Center, [10] Besançon Univeristy Hospital, , France, Department of Gastroenterology, [11] Guy's and St Thomas' NHS Foundation Trust, United Kingdom, IBD Unit, Department of Gastroenterology, [12] University Hospital of Caen, France, Department of Gastroenterology, [13] Newcastle University, United Kingdom, Translational & Clinical Research Institute, [14] St Georges University Hospital, United Kingdom, Gastroenterology, [15] AZ Delta, Belgium, Department of Gastroenterologie, [16] University of Lille, Inserm, CHU Lille, France, U1286 - INFINITE - Institute for Translational Research in Inflammation, [17] University Hospital of Amiens, France, Department of Gastroenterology, [18] University Hospital of Toulouse Rangueil, France, Department of Gastroenterology and Pancreatology, [19] Hopital Saint-Louis, France, Université de Paris, ECSTRRA - CRESS UMR1153, INSERM and SBIM, AP-HP, [20] Beaujon Hospital, APHP, Paris Cité University, France, Department of Gastroenterology, [21] Icahn School of Medicine at Mount Sinai, United States, Department of Gastroenterology, [22] Skåne University Hospital, Sweden, Department of Gastroenterology.

Introduction: In the SPARE trial, the discontinuation of infliximab (IFX) in patients with Crohn's disease (CD) in sustained remission under combination therapy (IFX and immunosuppressant therapy), was associated with a significantly higher relapse rate than when continuing combination therapy or discontinuing immunosuppressant therapy. However, a high proportion of patients rapidly recover remission when resuming treatment. The impact of this treatment strategy on functional disability, a major endpoint in assessing CD progression, has been poorly studied.
Aim: We aimed to compare the evolution of the IBD-disability index (IBD-DI) in patients continuing combination therapy, discontinuing IFX or immunosuppressant therapy.
Methods: The study of the evolution of the IBD-DI in the 3 groups (combination, IFX withdrawal, immunosuppressant withdrawal), between baseline and the end of study (2 years), was a pre-defined secondary endpoint of the trial. Changes in scores (between baseline and the end of study) were compared using Wilcoxon tests between the arms "combination group" versus "IFX withdrawal group" and between "immunosuppressant withdrawal group" versus "IFX withdrawal group".
Results: IBD-DI was available at baseline and at the end of study for 153 patients out of the 211 randomised in the SPARE trial between November 2015 and April 2019. Among patients included in the analysis, 46 were in the combination group (54% male, median age at randomisation of 38.5 years [IQR, 26-47]), 55 patients were in the IFX withdrawal group (60% male, median age at randomisation of 32 years [IQR, 25-42]) and 52 patients were in the immunosuppressant withdrawal group (50% male, median age at randomisation of 31 years [IQR, 25-42]). Among these, 30 patients had a relapse (6 [13%] of 46 in the combination group, 19 [34.5%] of 55 in the IFX withdrawal group, 5 [9.6%] of 52 in the immunosuppressant withdrawal group). Of 23 patients who had a relapse and were retreated or optimised according to protocol, remission was achieved in 21 patients (1 of 2 in the combination group, 18 of 19 in the IFX withdrawal group, and 2 of 2 in the immunosuppressant withdrawal group). The median IBD-DI at baseline was 12.5 (IQR, 5.36-21.43), without significant differences between the 3 groups. In the combination group, the median IBD-DI at baseline and at the end of study was 13.4 (IQR, 7.1-26.8) and 16.1 (IQR, 7.1-21.24), respectively. In the IFX withdrawal group, the median IBD-DI at baseline and at the end of study was 12.5 (IQR, 3.6-19.6) and 12.5 (IQR, 5.4-23.2), respectively. In the

immunosuppressant withdrawal group, the median IBD-DI at baseline and at the end of study was 10.7 (IQR, 5.4-18.8) and 12.5 (IQR, 4.9-23.7), respectively. There was no significant difference in terms of changes in IBD-DI between the arms "combination group" and "IFX withdrawal group" (p=0.56), or between the arms "immunosuppressant withdrawal group" and "IFX withdrawal group" (p=0.29).
Conclusions: In patients with CD in sustained steroid-free remission under combination therapy with IFX and immunosuppressant therapy, there was no difference in progression of disability over 2 years between those who continued combination therapy, stopped IFX or stopped the immunosuppressant with the possibility of recycling the medication after a relapse.

- I29 -

DIETARY EMULSIFIER K-CARRAGEENAN DOES NOT DIRECTLY AFFECT INTESTINAL PERMEABILITY IN ORGANOID-DERIVED EPITHELIAL MONOLAYERS FROM PATIENTS WITH CROHN'S DISEASE.
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Introduction: The dietary emulsifier carrageenan (CGN) is widely used to optimise the texture of processed foods such as ice cream, plant-based milk and processed meat products. However, CGN is suggested to play a role in IBD development by exerting pro-inflammatory effects and increasing intestinal permeability, as shown in immortalized cell lines and murine models. Specifically kappa-carrageenan (κ-CGN) has been shown to disrupt barrier function of intestinal epithelial cells.
Aim: In this study, we investigated if κ-CGN can directly increase intestinal permeability in organoid-derived epithelial monolayers from patients with Crohn's disease (CD).
Methods: Organoid cultures were derived from colonic biopsies of 5 patients with CD and seeded on Transwell® inserts to obtain epithelial monolayers. Two independent experiments were performed per patient (n = 10). Once a confluent monolayer was formed, non-inflamed and inflamed conditions were established by adding regular culture medium or inflammatory stimuli (100 ng/mL TNF-α, 20 ng/mL IL-1β, 1 μg/mL flagellin) to the basolateral side, respectively. The next day, both inflamed and non-inflamed monolayers were stimulated with 100 μg/mL κ-CGN on the apical side, or with regular culture medium as control. The basolateral side was also renewed with either the inflammatory stimuli or regular culture medium. Transepithelial electrical resistance (TEER) was measured after 24 and 48 hours of κ-CGN exposure to study permeability of the epithelium. Relative TEER (% change compared to baseline) was compared between controls and κ-CGN stimulated conditions (repeated measures ANOVA, Šídák's multiple comparisons correction).
Results: As expected, exposure to inflammatory stimuli on the basolateral side resulted in a significant reduction of TEER of the monolayers after 48 hours (+ 24 hours pre-stimulation), compared to the non-inflamed conditions (-22.54 ± 4.557 %, $p<0.0001$, paired t-test). After 24 hours of stimulation with κ-CGN, TEER did not significantly change in both the non-inflamed (p=0.90) and inflamed conditions (p=0.80), compared to the control conditions. Also after 48 hours, exposure to κ-CGN did not significantly affect the TEER in both non-inflamed (p=0.94) and inflamed (p=0.74) conditions. RNA analysis of the organoid-derived monolayers is ongoing to explore the inflammatory potential of κ-CGN and possible effects on mucus production.
Conclusions: The dietary emulsifier κ-CGN does not directly alter the permeability of the intestinal epithelium of CD patients. Further analysis of gene expression of inflammatory markers and mucus production is ongoing. Possible indirect effects, through alterations of the microbiota or immune cells, should still be explored.

- I30 -

REDUCTION OF MUCOSAL (ACTIVE) EOSINOPHILS, B CELLS AND T CELLS AFTER VEDOLIZUMAB THERAPY IN PATIENTS WITH ULCERATIVE COLITIS.
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Introduction: Patients with ulcerative colitis (UC) are often treated with biological therapies or small molecules. Knowledge about the impact of these therapies on the intestinal and peripheral blood immune cell composition is scarce.
Aim: Therefore, we investigated how advanced therapies modulate immune cell distribution in UC patients.
Methods: We included 30 UC patients (53% male, median age 42 years) who started a biological or small molecule. Before the first drug administration, mucosal colonic biopsies and a peripheral blood sample were obtained. At the end

of induction, colonic biopsies and peripheral blood were sampled again. Patients starting adalimumab (n=2), infliximab (n=3), vedolizumab (n=11), ustekinumab (n=6), ozanimod (n=2) and the JAK inhibitors filgotinib (n=3) and tofacitinib (n=3) were included. Endoscopic improvement was defined as a Mayo endoscopic subscore of 0-1 at the end of induction. From the biopsies, a single-cell suspension was made. Intestinal and circulating immune cells were characterized via flow cytometry. Statistical analysis was performed using a paired t-test.
Results: Independent of the mechanism of action, patients responding to therapy showed a decrease of colonic granulocytes (neutrophils ($p<0.0001$), basophils ($p<0.0001$) and eosinophils ($p=0.008$)), active eosinophils ($p=0.002$), B cells ($p=0.05$), regulatory T cells ($p<0.0001$) and T helper (Th) 2 cells ($p=0.02$), balanced with an increase of Th1 cells ($p=0.03$). In peripheral blood, eosinophils increased in patients not responding to therapy ($p=0.05$). Furthermore, we observed that only patients starting vedolizumab (n=11) showed a decrease in colonic eosinophils ($p=0.02$), active eosinophils ($p=0.002$), B cells ($p=0.03$) and T cells ($p=0.004$). Considering only non-vedolizumab patients (n=19), we did not observe this effect.
Conclusions: UC patients responding to advanced therapies showed a different intestinal immune cell distribution compared to non-responders, regardless of MOA. Vedolizumab therapy furthermore decreased several mucosal immune cell subsets that migrate to the gut through α4β7-MAdCAM-1 binding. While the effect of vedolizumab on B cells and T cells was previously described, we have now potentially identified an additional eosinophil-reducing effect in the colon.

- I31 -

UNRAVELING THE TRANSCRIPTIONAL DYNAMICS OF ENTERIC GLIAL CELLS IN INTESTINAL HOMEOSTASIS AND DISEASE. S. Santhosh (1), L. van Baarle (1), V. De Simone (1), S. Abdurahiman (1), A. Zouzaf (1), M. Hao (2), L. Stamp (2), G. Matteoli (1) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism, [2] University of Melbourne, Parkville, Australia, Department of Anatomy and Physiology.

Introduction: In individuals with a genetic and environmental predisposition, such as altered microbiota, previous infections, or exposure to chemicals and pollutants, the regulation of intestinal homeostasis becomes compromised. This results in persistent and recurring immune activation, leading to the development of gastrointestinal disorders such as inflammatory bowel disease (IBD) and colorectal cancer (CRC). Recently, enteric glial cells (EGCs), the non-neuronal counterpart of the enteric nervous system have been recognized as a crucial player in both intestinal homeostasis and inflammation. Recent studies explore the capabilities and plasticity of EGCs beyond their well-known conventional function of supporting enteric neurons. Indeed, EGCs are able to respond to inflammatory signals, resulting in alterations in their morphology and function. Research suggests that EGCs favor the resolution of intestinal inflammation. Interestingly, a few studies also show that, in CRC, EGCs promote tumor development and progression. However, the mechanisms governing their functions remain largely unexplored. Furthermore, the comprehensive understanding of the EGC diversity and their transcriptional and functional characteristics in health and disease is still limited.
Aim: To study the diversity in EGC populations and their role in homeostasis and disease. We will study the transcriptional mechanisms by which EGCs play a role in the resolution of intestinal inflammation and in promoting the development of tumors in CRC.
Methods: To study the diversity and role of EGCs in IBD, the human single-cell RNA-sequencing (scRNA-seq) datasets of IBD patients and healthy individuals were obtained from published studies. ScRNA-seq data analysis was performed using the standard Seurat pipeline. For comparison across datasets, harmony batch correction was performed. To explore the enriched pathways in the EGCs subsets, GO-overrepresentation analysis (ORA) was implemented using clusterprofiler R package. To understand transcriptional and functional characteristics of EGCs in CRC, we used mouse orthotopic tumor model generated by colonoscopy-guided submucosal injection of MC38 to C57BL/6J mice. To mimic the EGCs in the CRC tumor microenvironment, we implemented an in-vitro tumor EGC model using mice embryonic neurosphere-derived EGCs treated with supernatant of digested orthotopic tumors. To identify the co-expression of gene modules in tumor EGCs compared to healthy EGCs, weighted gene correlation network analysis (WGCNA) was performed on the bulk RNA sequencing data of the in-vitro tumor EGCs (untreated/treated with tumor-conditioned media). To understand the relevance of EGCs as a prognostic factor, we collected the RNA-seq dataset of colorectal cancer patients from the TCGA database, and survival analysis was performed by hierarchically clustering the patients based on the expression of well-known EGC-specific genes.
Results: The human scRNA-seq data analysis shows that, in IBD, the variation in EGCs subsets depends on the anatomical location, homeostasis, and inflammation. We have identified a subset of EGCs expressing CD74 and S100A4 which is absent in the ileum compared to the colon. This cluster has an upregulation of HLA-DR genes, which could be due to the presence of diverse microbiota in the colon. While the SOX10+ FOXD3+ glia cluster was highly enriched in non-inflamed samples of IBD patients, the CEBPD+ glia cluster was mainly present in the samples from healthy individuals. To characterize the EGCs in the CRC tumor microenvironment, we analyzed the bulk RNA-seq data of tumor EGCs. The results suggest that tumor EGCs are distinct from healthy EGCs. The WGCNA and GO-ORA revealed the difference in transcriptional and functional characteristics of tumor EGCs compared to healthy EGCs. We found that glial cells acquire a reactive phenotype in the tumor microenvironment and express inflammatory genes such as Lcn2,

Timp1, Ccl2, Il6. The GO-ORA of the tumor EGC-related WGCNA gene modules revealed that IL1α and IL1β pathways are over-represented in the murine tumor EGCs. The survival analysis suggests that the patients with high expression of EGC-specific genes have lower overall survival probability compared to patients with low expression of EGC genes.
Conclusions: Here we have identified differences in the distribution of EGC population in homeostasis and disease and their functional and transcriptional differences. Our data further corroborate the idea that the plasticity of EGCs enables them to respond to microenvironmental cues and acquire disease-specific phenotype while contributing to disease pathogenesis.

- I32 -

JAKNE: JAK INHIBITOR ASSOCIATED ACNE, A REAL-LIFE SINGLE-CENTER EXPERIENCE. E. De Dycker (1), S. Vermeire (1), M. Ferrante (1), T. Lambrechts (1), A. Paps (1), P. Geens (1), E. Loddewijkx (1), J. Sabino (1), T. Hillary (2), B. Verstockt (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Dermatology.

Introduction: Three Janus kinase (JAK) inhibitors, tofacitinib (TFC), filgotinib (FIL) and upadacitinib (UPA), have been approved for treatment of Crohn's disease (CD) and/or ulcerative colitis (UC). During the IBD registrational trials, acne was reported as adverse event (AE) in 5-7% of UPA treated patients, but not in the FIL and TFC programs. Hence, we assessed the prevalence of JAK inhibitor associated acne in a real-life cohort.
Aim: We aimed to assess the prevalence of JAK inhibitor associated acne in a real-life cohort.
Methods: All patients initiating JAK inhibitors for active moderate-to-severe CD or UC at our center were included. Patients were prospectively monitored at prespecified timepoints, and specifically assessed for AEs including acne. Affected patients completed a visual analogue scale (VAS) to assess the impact of acne on their quality of life. All pictures of skin lesions were assessed by a dermatologist specialized in inflammatory skin diseases.
Results: In total, 46 patients initiated TFC, 40 FIL and 79 UPA. None of the TFC or FIL treated patients reported new onset of acne. Instead, 17 (21.5%) patients (9 CD, 8 UC; median [IQR] age 28.2 [25.2-45.0]; 47.1% female) spontaneously reported acne during UPA therapy. Most (89.5%) reported new onset of acne, while 2 (10.5%) mentioned a deterioration of existing acne during UPA induction. Previous acne during adolescence was reported by 46.2%. Lesions were present in the face (82.3%), back (23.5%), chest (23.5%) and scalp (11.8%). The acne phenotype included inflammatory papules in all patients, but also pustules (66.7%), nodules (33.3%), cysts (11.1%) and comedones (11.1%) were observed. A median VAS score of 5.5 [5.0-7.0] highlighted the impact on the patient's quality of life, though no patient interrupted UPA due to acne. Six (35.2%) patients were referred to a dermatologist for acne. Most patients (82.4%) received topical skin therapy during UPA induction based on a standard operation procedure approved by the dermatologist and communicated via the IBD nurses. Three patients (17.6%) received antibiotics during UPA induction because of acne. During UPA maintenance, 5 patients (29.4%) reported resolution of skin problems with only 1 requiring continued skin therapy. Ten patients (58.7%) continued topical skin therapy during maintenance, with 4 of them requiring continued antibiotic treatment for at least 3 months. A single patient was deescalated from UPA 30mg to 15mg QD because of severe acne, with little improvement.
Conclusions: In this real-world experience, JAK inhibitor associated acne was uniquely linked to UPA, occurring in one fifth of patients. This is more prevalent than observed in the registrational trials. Awareness and patient education are therefore important, as well as early referral to the dermatologist for appropriate treatment.

- I33 -

SIMPLIFIED MARIA SCORE DOES NOT PREDICT LONG-TERM OUTCOMES IN CROHN'S DISEASE PATIENTS UNDERGOING MODIFIED SIDE-TO-SIDE STRICTUREPLASTY FOR EXTENSIVE ILEITIS. I. De Greef (1), G. Bislenghi (2), M. Lenfant (3), S. Verstockt (3), I. Terrasson (2), B. Verstockt (4), J. Sabino (4), M. Ferrante (4), D. Vanbeckevoort (5), A. D'Hoore (2), S. Vermeire (4) / [1] KUL - University of Leuven, Leuven, Belgium, Chronic Diseases and Metabolism (CHROMETA), [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Abdominal Surgery, [3] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [5] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Radiology.

Introduction: Strictureplasty techniques were developed to limit the risk of short bowel syndrome in Crohn's disease (CD) patients with affected small intestine. In the setting of extensive small bowel disease, long strictures might be treated with modified side-to-side isoperistaltic strictureplasty (SSIS).
Aim: We studied long-term outcomes in patients who underwent SSIS and evaluated if radiological features on MR enterography (MRE) are predictive of long-term outcome.
Methods: This retrospective study included CD patients who underwent SSIS between 2012 and 2022 in our tertiary IBD center, for whom preoperative and six-month postoperative MRE were routinely performed. Simplified MARIA (MARIAs) score, considering wall thickness, edema, fat stranding and ulcers (score >1 indicates active CD; maximum

5) was used. Improvement in maximal wall thickness was defined as a decrease of at least 30% from baseline. Deep remission was defined as absence of symptoms and endoscopic remission (mRutgeerts score ≤i1), and clinical recurrence as occurrence of new symptoms confirmed by endoscopy (mRutgeerts score ≥i2b) or radiology (new strictures and/or inflammation) requiring treatment. All clinical data were collected from medical records. The correlation between recurrence and features within the MARIAs score was assessed.
Results: Thirty CD patients underwent (modified) SSIS and had pre- and six-month postoperative MRE. The median [IQR] length of affected bowel was 40.0 [30.0-52.0] cm. Immediately after surgery, 13 (43.3%) patients were continued or initiated on advanced therapy. Over a median [IQR] follow-up of 7.4 [3.3-9.3] years, 17 (56.7%) patients showed clinical recurrence of whom 6 (20.0%) eventually needed surgical reintervention. Deep remission was observed in 8 (26.7%) patients. Preoperatively, all patients had the maximum MARIAs score of 5. After surgery, the median [IQR] change in MARIAs score was 0.0 [0.0-0.8]. Cox regression analysis showed no association between decrease in overall MARIAs score, nor the separate components of this score, with clinical or surgical recurrence free survival. Wall thickness decrease of >30%, as observed in 15 (50%) patients, did not predict long-term recurrence free survival, although a trend was seen for clinical recurrence free survival (p=0.098). Three patients showed normalization of MARIAs score six months postoperatively and all three showed no recurrence thereafter. None of the clinical variables collected showed significant association with recurrence, except for immediate postoperative initiation of advanced therapy which had a 70% protection from clinical recurrence [p=0.036 / HR 0.3 (0.097-0.92)].
Conclusions: Long-term follow-up of patients with CD undergoing SSIS showed that 57% of patients had clinical recurrence and 20% needed surgical reintervention. The MARIAs score was not predictive of long-term postoperative clinical or surgical recurrence after SSIS surgery as most features of the score remained unaltered. These shortcomings of the MARIAs score should be addressed when designing improved scoring tools.

- I34 -

THE COMPARATIVE EFFECTIVENESS AND SAFETY OF DIFFERENT BIOLOGICS IN YOUNG (<60 YEARS) VERSUS ELDERLY (≥60 YEARS) PATIENTS WITH IBD: RESULTS FROM A REAL-WORLD EXPERIENCE AT A BELGIAN TERTIARY CENTRE. L. Deroo (1), M. Truyens (1), J. Geldof (1), S. Akhayad (1), G. Dewitte (1), E. Glorieus (1), T. Lobaton (1) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology and Hepatology.

Introduction: The therapeutic armamentarium for inflammatory bowel disease (IBD) is rapidly expanding as well as the number of elderly patients with IBD. Given the frailty of this subpopulation, it is of increasing importance to have data on the efficacy and safety of different therapies in this cohort.
Aim: To assess the efficacy and severe adverse event (SAE) rate of different biologics in young (<60 years (yr)) versus elderly patients with IBD (≥60 yr) in a real-world tertiary cohort.
Methods: A retrospective monocentric study was performed at the Ghent University Hospital. Patients starting anti-TNF, ustekinumab (UST) or vedolizumab (VDZ) from 01/2018 to 06/2021 with follow-up until 12/2022 were included. Co-primary endpoints after induction and after 1 yr of therapy were: clinical response (CRp) and remission (CRm), biochemical response (BRp) and remission (BRm) and endoscopic response (ERp) and remission (ERm). The secondary endpoint was treatment survival. Severe adverse events (SAE) were defined as intestinal resection (IR), IBD-inflammation related hospitalization (IBD-hosp), IBD-treatment related hospitalization (e.g. infections) (treat-hosp), malignancy and death. Multivariate logistic regression (MLR) and Cox regression model (CRM) were applied to assess potential risk factors (RF).
Results: A total of 267 patients were included: 234 patients <60 yr and 33 elderly patients. At baseline, the elderly patients had a significant higher age at IBD diagnosis (56 yr vs 24 yr, P=0.002), more moderate to severe comorbidities (57.6%% vs 3.4%, P<0.001), a higher calprotectin level at start (1187.5 vs 467.5, P=0.030) and a longer disease duration (10 vs. 5 yr, P=0.039). Younger patients were more often under combination therapy with an immunomodulator (IMM) (42.3% vs 21.2%, P=0.020). The distribution of biologic therapy started was significantly different (P=0.026): more younger patients started anti-TNF, more elderly patients VDZ and UST. After induction, CRp (P=1.000), CRm (P=0.079) and BRp (P=0.059) were not significantly different between both groups. BRm was significantly higher in younger patients (135/199 (67.8%) vs 10/23 (43.5%), P=0.020), but younger age was not significantly associated with BRm in the MLR (aOR 2.47, [0.97-6.31], P=0.059). Patients with Crohn's disease had a higher odds of reaching BRm (aOR 2.34, [1.24-4.44], P=0.009) as well as patients treated with adalimumab (aOR 3.08, [1.10-8.64], P=0.033). Univariate analysis showed no significant difference for ERp (P=0.207) or for ERm (P=0.523). After one year of therapy, no difference was seen for CRp (P=0.228), CRm (P=1.000), BRp (P=0.343), BRm (P=0.353), ERp (P=0,663) and ERm (P=0.771). There was no significant difference regarding treatment survival for both age groups (aHR 0.701, [0.346-1.420], P=0.324, as well as for reason to stop biologic (P=0.336). Regarding SAEs, a higher rate was seen for elderly patients (63/234 (26.9%) vs. 15/33 (45.5%), P=0.028). CRM showed elderly age as a RF for SAE (aHR 1.86, [1.01-3.44], P=0.047), adjusting for type of biologic, use of systemic corticosteroids or IMM, previous IR, disease duration and number of previous biologics used. Regarding different subtypes of SAE, univariate analysis showed no significant difference for IR (P=0.503), IBD-hosp (P=0.714), specific IBD related SAE (P=0.480), malignancy (P=0.162) and death (P=1.000).

Treat-hosp was significantly higher in elderly patients (12/234 (5.1%) vs. 8/33 (24.2%), P=0.001), and elderly age was significantly associated with Treat-hosp in the CRM (aHR 5.01, [1.92-13.04], P<0.001).
Conclusions: No difference was seen regarding efficacy of different biologics in younger versus elderly patients. SAE rate was higher in elderly patients.

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- K01 -

ULTRA-PROCESSED FOOD INTAKE DOES NOT CORRELATE WITH PAEDIATRIC MASLD IN THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY. M. Buytaert (1), F. Depoorter (2), Z. Cosijn (2), L. Devisscher (3), S. Raevens (1), X. Verhelst (1), H. Van Vlierberghe (1), A. Geerts (1), D. Declercq (1), R. De Bruyne (1), S. Lefere (1) / [1] Ghent University, Ghent, Belgium, Department of Internal Medicine and Pediatrics, [2] Ghent University, Ghent, Belgium, Faculty of Medicine and Health Sciences, [3] Ghent University, Ghent, Belgium, Department of Basic and Applied Medical Sciences.

Introduction: With the increasing prevalence of obesity in the western world, metabolic dysfunction-associated liver disease (MASLD) has become a major concern. Also in the paediatric population, the estimated MASLD prevalence has risen to 5-10% at present. It is important to identify the underlying risk factors to implement effective preventive measures. In particular, previous studies have shown a link between some food compounds, such as high fructose intake, with MASLD. Furthermore, food products in the western diet are increasingly becoming ultra-processed (UPF), meaning that they are (mostly) industrially formulated, contain additives, and are ready-to-eat and hyperpalatable. Recently, Zhao et al. have investigated the link between UPF intake and MASLD in the National Health And Nutrition Examination Survey (NHANES) cohort of 2017-2018 for all ages. They have reported a positive association between UPF intake and odds of MASLD in adolescents and adults, although the former was not studied in much detail.
Aim: In this study, we aimed to examine the link between UPF intake and MASLD in the adolescent population (12 – 18 years) of the NHANES pre-pandemic cohort (2017 – March 2020).
Methods: Participants of the NHANES pre-pandemic cohort aged 18 years or younger with complete data on food intake on two separate days and a complete, valid, liver examination by the FibroScan® 502 V2 Touch were included in our study cohort. To address under- and overreporting of food intake, a known problem in nutritional research, we have calculated the total energy expenditure (TEE) for all participants by multiplying basic metabolic rate and physical activity level. Participants with a total energy intake lower than 0,8 times or higher than 1,5 times the TEE were excluded from the analysis. To assess the possible link between UPF intake and MASLD, we have calculated the percentage of total energy intake (in kilocalories) of all food products, classified according to the NOVA classification, in which UPFs are categorized as NOVA IV. This classification was performed based on the reported food codes of the Food and Nutrient Database for Dietary Studies. The Controlled Attenuation Parameter (CAP) was in the primary analysis used as a measure for MASLD, with a cut-off of 248 dB/m for steatosis and 300 dB/m for severe steatosis. Data were analysed using the Kruskal-Wallis and chi² test, and Spearman correlation coefficient. Structural equation modelling was used to better quantify the causal connection between UPF and liver steatosis, estimated through latent variables.
Results: Analysis was performed on 649 participants, of whom 496 had no steatosis, 108 light to moderate steatosis and 45 severe steatosis. Groups were balanced with respect to age and biological sex, whereas weight and BMI z-scores increased with worsening liver steatosis. The correlation coefficient between UPF intake and CAP was 0,063 (p=0,107). The median proportion UPF intake in these groups was 74,4% (interquartile range 61,3-86,1), 76,6% (63,4-87,0) and 79,2% (64,3-85,8), respectively, which does not differ significantly (p=0,363). Total energy intake however differed significantly, with a median of 1904 kilocalories (kcal) in the no steatosis group, 2061 kcal in the light to moderate steatosis group and 2258 kcal in the severe steatosis group (p<0,001). Performing the analysis with energy-adjusted gram intake, a limited increase of 1,1dB/m (0,1-2,1) in CAP value is observed per additional 100 grams UPF intake per day (p=0,038). There were no significant changes in liver stiffness (p=0,521) or serum alanine aminotransferase (ALT) (p=0,647). Furthermore, assessing the correlation between UPF intake and liver steatosis by structural equation modelling similarly yielded a weak and non-significant correlation of 0,026.
Conclusions: No clinically relevant association between UPF intake and MASLD in adolescents in the NHANES pre-pandemic cohort could be demonstrated. However, the methodological difficulties in obtaining nutritional data, as well as the high UPF intake on the group level call for caution in interpreting the pathophysiological importance of UPF. Our results nonetheless confirm that total energy intake is an important contributor to paediatric obesity and MASLD.

- K02 -

LONG-TERM MAINTENANCE OF RESPONSE AND IMPROVED LIVER HEALTH WITH MARALIXIBAT IN PATIENTS WITH PROGRESSIVE FAMILIAL INTRAHEPATIC CHOLESTASIS (PFIC): 2-YEAR DATA FROM THE MARCH-ON STUDY. E. Sokal (1), A. Miethke (2), A. Moukarzel (3), G. Porta (4), J. Esquer (5), P. Czubkowski (6), F. Ordonez (7), M. Candusso (8), A. Aqul (9), R. Squires (10), D. D'Agostino (11), U. Baumann (12), L. D'Antiga (13), N. Kasi (14), N. Laborde (15), C. Arikan (16), C. Lin (17), S. Gilmour (18), N. Mittal (19), F. Chiou (20), S. Horslen (21), W. Huber (22), T. Nunes (23), A. Lascau (23), L. Longpre (23), D. Mogul (23), M. Baek (24), P. Vig (23), V. Hupertz (25), R. Gonzalez-Peralta (26), U. Ekong (27), J. Hartley (28), N. Laverdure (29), N. Ovchinsky (30), R. Thompson (31) / [1] UCLouvain, Cliniques Universitaires St Luc, Belgium, Pediatric Hepatology, [2] Cincinnati

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Introduction: Progressive familial intrahepatic cholestasis (PFIC) is a group of genetic disorders resulting in disrupted bile composition, cholestasis, and pruritus. Maralixibat (MRX) is a minimally absorbed ilea I bile acid transporter inhibitor which prevents enterohepatic bile acid recirculation. In the 26-week placebo-controlled MARCH Phase 3 study, MRX at 570 μg/kg BID demonstrated significant improvements in pruritus, serum bile acids (sBA), total bilirubin (TB) and growth in patients across the broadest range of PFIC types studied to date.
Aim: We report on long-term maintenance of effect of up to 2 years of treatment with MRX in MARCH-ON, an open-label, long-term extension study of MARCH.
Methods: Long-term maintenance of response was assessed for patients who were originally randomised to receive MRX in MARCH and continued with treatment in MARCH-ON (MRX-MRX group: n=33; BSEP [n=14], FIC1 [n=7], MDR3 [4], TJP2 [6], MYOSB [2]), and for patients who received placebo (PBO) in the MARCH study and switched to open-label MRX in MARCH-ON (PBO-MRX group: n=27; BSEP [n=14], FIC1 [n=6], MDR3 [n=5], TJP2 [n=1], MYO5B [n=1]). Assessments included: pruritus, sBA, TB, growth z-scores, and incidence of treatment-emergent adverse events (TEAEs). Baseline (BL) was defined as the start of MRX for each group.
Results: For the MRX-MRX group, the median (min, max) time on MRX was 638 days (108, 1023). 13 of 33 patients reached Week 104 at time of analysis. Significant improvements observed in the first 26 weeks of the MARCH study were sustained through Week 104 in MARCH-ON for pruritus (-2.03, $p<0.0001$), sBA (-166 μmol/L, $p=0.003$), TB (-1.6 mg/dL, $p=0.02$), and growth (height z-score: +0.40, $p=0.046$; weight z-score: +0.52, $p=0.01$). In the PBO-MRX group, the median time on MRX was 475 days (72, 720). 18 of 27 patients reached Week 52 of MRX treatment at time of analysis. Significant improvements through Week 52 for pruritus (-1.1, $p=0.0001$), sBA (-71 μmol/L, $p=0.03$), and growth (height z-score: +0.37, $p=0.01$; weight z-score: +0.32, $p=0.03$) were in line with observations from the initial MARCH MRX group. Additionally, numeric reductions in TB (-0.4 mg/dL; $p=0.7$) were observed. No new safety signals were identified. The most common TEAEs were GI-related with diarrhoea (50%) being mostly mild and transient.
Conclusions: Significant and sustained improvements in pruritus, sBA, TB, and growth are observed with up to 2 years of MRX treatment across the broadest range of genetic PFIC types studied to date. These data suggest overall improved liver health with MRX treatment which can be maintained long-term.

- K03 -

NUTRITIONAL MANAGEMENT OF HIGH-OUTPUT ILEOSTOMIES IN PEDIATRIC PATIENTS. M. Awouters (1), I. Hoffman (2), T. Vanuytsel (3), P. De Bruyne (4), K. Huysentruyt (5), K. Van Hoeve (6) / [1] KUL - University of Leuven, Leuven, Belgium, pediatrics, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, pediatrics, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [4] University Hospital Ghent (UZ Gent), Gent, Belgium, Pediatrics, [5] KidZ Health Castle, UZ Brussel, Jette, Belgium, Pediatrics, [6] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Pediatrics.

Introduction: Children with high-output ileostomies (HOI) have a high risk of complications, including dehydration, electrolyte disturbances and malnutrition. Adequate nutritional management is crucial.
Aim: The aim of this narrative review is to give an overview of the literature and to provide recommendations for the nutritional management of pediatric patients with HOI.
Methods: We conducted an eleborate research of Medline. Recommendations were made based on the evidence found and discussed with multiple experts on intestinal failure.
Results: A cut-off for pediatric HOI at 20mL/kg/day is proposed. At its occurrence, organic causes need to be sought and treated if found. For all patients, ad hoc intravenous compensations should be administered to prevent dehydration. Electrolyte and micronutrient deficiencies should be monitored and supplemented when found. In neonates and infants with a HOI, bolus feeds with breastmilk or hydrolyzed formula are the preferred initial dietary option. When not tolerated or when high-output persists, a trial with amino acid formula or continuous tube feeding can be considered. In older children, an enteral fluid restriction should be installed with a preference for isotonic or slightly hypotonic glucose-electrolyte solutions. A high calorie, high protein, low insoluble fiber, moderate fat diet with reduction of simple carbohydrates should be promoted. General advice regarding eating behavior needs to be given.
Conclusions: The evidence available on the nutritional management of ileostomies in pediatric patients is scarce. Clinical research in children is needed to be able to provide more evidence-based guidelines.

- K04 -

RELIABILITY OF UPDATED KIDZ HEALTH CASTLE FORMULA (KHC-F V2) USED FOR PROPER PROBE POSITIONING OF A MULTICHANNEL INTRALUMINAL IMPEDANCE PH MONITORING (MII-PH). H. Delcourt (1), K. Huysentruyt (2), Y. Vandenplas (2) / [1] KidZ Health Castle, UZ Brussel, Jette, Belgium, Pediatrics, [2] KidZ Health Castle, UZ Brussel, Jette, Belgium, Pediatric Gastroenterology, Hepatology and Nutrition.

Introduction: The KidZ Health Castle formula (KHC-F) is a user friendly formula for correct probe positioning of a multichannel intraluminal impedance pH monitoring (MII-pH). The KHC-F resulted in 64.9% of the children having a correct probe position (ρ=0.91 with radiological position). A post-hoc correction to the KHC-F, labelled KHC-F v2, was developed by Vandercuys et al. The KHC-F v2 is based on the mean error (-0.44cm) of the original KHC-F by distracting 0.5cm of the insertion length obtained with the original KHC-F.
Aim: Our aim is to test the reliability of the updated KHC-Fv2 as a standard formula for estimating the consensus position of the pH probe.
Methods: A retrospective cohort study analyzing data on MII-PH position of all patients between one month and 18 years old who were referred for MII-pH to the KidZ Health Castle (UZ Brussel) between October 11, 2022 and August 28, 2023. A total of 84 children were included. A margin of error between KHC-F v2 and radiological position up to one centimetre above or below target position was accepted. Statistical analysis was done using R v 4.0.3 and included Bland Altman plots and spearman correlations.
Results: A strong correlation was observed between the probe position calculated with the KHC-Fv2 formula and the radiological position (ρ=0.97; $p<0.001$). The mean difference between the KHC-Fv2 and the target position was +0,25 cm cranially (lower limit -3.1cm, upper limit +3.5cm). For 67.9% children the KHC-Fv2 insertion length fell within the accepted difference of +/- 1 cm from the target position. This percentage increased when limiting the formula to children younger than 1 year of age (79.5%) or shorter than 100 cm (74%).
Conclusions: The KHC-F v2 outperforms the KHC-F, demonstrates good agreement with radiological target position and reduces the need for a second radiological control after repositioning of the probe especially in children younger than one year of age or children shorter than 100cm.

- K05 -

UPDATED ESPGHAN 2023 GUIDELINES ON EOSINOPHILIC OESOPHAGITIS IN CHILDREN. S. Vande Velde (1), O. Bauraind (2), K. Huysentruyt (3) / [1] Ghent University Hospital, Ghent, Belgium, Pediatric Gastroenterology, [2] Clinique du MontLégia - CHC Groupe Santé, Liège, Belgium, Pediatric Gastroenterology, [3] Vrije Universiteit Brussel (VUB), Jette, Belgium, Pediatric Gastroenterology.

Introduction: ESPGHAN published a guideline on eosinophilic oesophagitis (EoE) in children in 2014; however, due to the rapid evolution of knowledge an update was deemed necessary.
Methods: A consensus group of pediatric gastroenterologists from the ESPGHAN Working Group on Eosinophilic Gastrointestinal Diseases (ESPGHAN EGID WG) reviewed the recent literature and proposed statements and recommendations on 28 relevant questions about EoE (1). The literature search was then performed between October 1, 2014, and December 31, 2021, using PubMed, MEDLINE, EMBASE, Cochrane Library, and Scopus databases. Evidence was graded according to GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology to rate the quality of evidence (high, moderate, low, or very low quality). Statements and recommendations were discussed in virtual meetings and an electronic vote was held to rate each of them using a 6-point scale. The

statements and recommendations that did not achieve consensus were reformulated and re-voted until agreement was reached.
Results: WHAT IS KNOWN • EoE is a chronic non-IgE mediated inflammatory disease. • There is a discrepancy between symptoms and endoscopic and histologic features. • Allergy testing is of no value in deciding which foods to eliminate. • EoE may cause esophageal stenosis even in pediatric patients. • Maintenance therapy after induction is necessary. WHAT IS NEW • The diagnosis of EoE no longer requires failure of a PPI trial. • Validated questionnaires are available for assessing symptoms and QoL and should be incorporated in the management of children with EoE. • The use of endoscopic and histologic scores improves diagnostic efficacy and helps monitor the inflammatory process. • PPI, topical steroids and diet are all valuable first-line treatments for EoE. • Second-line treatment is the combinations of two of the above valuable treatment options. • Systemic steroids may be helpful in the treatment of severe esophageal strictures. • New biologic agents may be helpful in treating patients not responding to or intolerant to second-line treatment. • A discrepancy between eosinophil depletion and symptomatic improvement requires reassessment of non-eosinophil-dependent inflammation. • Implementation of programs for transition to adult care must be considered and started well before patients reach adulthood. (1) Diagnosis and management of eosinophilic esophagitis in children: an update from the European society for Pediatric Gastroenterology, hepatology and Nutrition (ESPGHAN). Accepted by JPGN.

- K06 -

RECURRENT INFANTILE HYPERTROPHIC PYLORIC STENOSIS IN A 5 WEEKS OLD BOY: CASE REPORT AND LITERATURE REVIEW. M. Schils (1), H. Haidar (1), K. Kalliroy (1), A. Poupalou (1), C. Zamfir (1), H. Reusens (1) / [1] HUDERF, Brussels, Belgium, ULB.

Introduction: Recurrent pyloric stenosis (RPS) is a very rare condition that occurs after an initially successful pyloromyotomy for hypertrophic pyloric stenosis. Over the last decade, the number of reported cases of recurrent pyloric stenosis has increased considerably. Given the rarity of this condition and the paucity of existing literature on the subject, there is a certain diagnostic difficulty, particularly at ultrasound level, where it is difficult to differentiate a true recurrence of pyloric stenosis from an initial incomplete post-pyloromyotomy scar.
Aim: Through a thorough examination of all instances of recurrent pyloric stenosis outlined in the literature, incorporating their ultrasound information, our aim was to establish a strong foundation for precisely identifying and confirming authentic recurrent pyloric stenosis.
Methods: We presented a new case report of a RPS. A systematic literature review was performed to characterize the diagnosis of this pathology and to report on all cases previously described in literature.
Results: We identified a total of 14 patients (median age : 40,5 days with an average of 24.5 days of symptom-free interval before the RPS; 71% male). The length of the pylorus on ultrasound appeared to increase or remain above 18 mm during RPS, in contrast to pyloric stenosis, pyloromyotomy results in a reduction in length. RPS seemed to occur more frequently when the first pyloromyotomy was performed at an early age (median age: 18 days).
Conclusions: The diagnosis of true RPS could be made through the use of Upper GI series and ultrasound imaging specifically through the length measurements of the pylorus. However, further research should be done on this subject to prove its sensitivity

- K07 -

THE COW'S MILK-RELATED SYMPTOM SCORE (COMISS) IN HEALTHY EGYPTIAN, INDONESIAN AND BRAZILIAN INFANTS. N. Knockaert (1), K. Huysentruyt (2), W. Bahbah (3), H. El Zefzaf (3), B. Hegar (4), J. Motta Franco (5), V. Santos Macedo (5), S. Vieira (5), Y. Vandenplas (2) / [1] KidZ Health Castle, UZ Brussel, Jette, Belgium, pediatrics, Vrije Universiteit Brussel (VUB), [2] KidZ Health Castle, UZ Brussel, Jette, Belgium, Pediatrics, Vrije Universiteit Brussel (VUB), [3] Menoufia University, Shebin El-Kom, Egypt, Menofia Governorate, Egypt, Department of Pediatrics, Faculty of Medicine, [4] Universitas Indonesia, awa Barat, Indonesia, Department of Child Health, Faculty Medicine, [5] Federal University of Sergipe, Sergipe, Brazil, Reference Center for Food Allergy of Sergipe.

Introduction: The Cow's Milk-Related Symptom Score (CoMiSS) raises awareness of Cow's Milk Allergy (CMA) symptoms and has a cut-off of ≥ 10 for a "positive test". CoMiSS in healthy infants needs to be determined as the score does not return to 0 after elimination diet [PMID: 26770708]. The median and mean (SD) CoMiSS in healthy European infants were 3.0 and 3.7 (2.9), respectively [PMID: 30020980].
Aim: This study aims to establish normal CoMiSS values in healthy Egyptian, Indonesian and Brazilian infants.
Methods: In this prospective cross-sectional study pediatricians determined the CoMiSS in healthy infants ≤ 12 months. Infants seeking medical help due to CMPA symptoms, infants with any known or suspected diseases, with preterm delivery or infants under medication or food supplements (except for vitamins) were excluded.
Results: In Egypt a total of 808 infants were included (50.7% boys). The median (Q1;Q3) CoMiSS was 5 (5;6) and the mean (SD) was 5.2 (1.4). The 95th percentile was 7. There was no significant difference in median CoMiSS according to

gender (p=0.621) or exclusively breastfeeding (p=0.603). In Indonesia, a total of 286 infants were included (50.7% boys). The overall median (Q1;Q3) and mean (SD) CoMiSS were respectively 1.5 (0;4) and 2.3 (2.4). The 95the percentile was 7. No significant difference in CoMiSS was seen according to sex (p=0.212) or exclusive breastfeeding (p=0.397) In Brazil, 101 infants were included (60.4% boys). The median (Q1;Q3) CoMiSS score was 4 (4;6) and the mean (SD) was 5.24 (2.2) with a 95th percentile of 10.9. No significant difference in CoMiSS was seen according to sex (p=0.579) or exclusive breastfeeding (p=0.344). Age (OR -0,061, 95% CI -0,089;-0.033, p<0.001) and country (OR 2,96 95% CI 2.56;3.379, p<0.001; OR 3,05 95% CI 2,80;3,29, p<0,001) were significant independent predictors for a change in mean CoMiSS in a multiple linear regression model (r2=0.34)

Conclusions: In healthy Egyptian infants the median CoMiSS was 5, in healthy Indonesian infants the median CoMiSS was 1.5, whereas for healthy Brazilian infants the median CoMiSS was 4. There was a significant difference in CoMiSS according to age and country.

BELGIAN WORKING GROUP OF PROCTOLOGY

- M01 -

SCREENING FOR ANAL DYSPLASIA IN HIV-POSITIVE INDIVIDUALS: CURRENT GUIDELINES AND IMPLEMENTATION.

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Introduction: Anal cancer, though relatively rare, poses a significant health concern with an increasing incidence. This research delves into the screening for anal cancer, exploring current methodologies and potential enhancements. By shedding light on at-risk populations, screening modalities, and precursor lesion detection, the aim is to provide valuable insights into cancer prevention, particularly focusing on HIV-positive MSM (men who have sex with men), given their substantially higher risk of anal cancer.

Aim: This study aims to investigate the process of screening for anal cancer in HIV-positive individuals at UZ Gent. Specifically, it examines precursor lesions found in anal cytology, their correlation with findings in high-resolution anoscopy (HRA), and the diagnostic value of HR-HPV typing in ASCUS lesions.

Methods: A literature review was conducted, supplemented by a retrospective analysis of patient data at UZ Gent. The study evaluated 248 HIV-positive patients, predominantly MSM, who underwent cytology. Follow-up cytologies and HRAs between October 2010 and October 2023 were analyzed, encompassing a total of 508 cytologies and 316 HRAs.

Results: The average age of the population was 49 years, with 94% being MSM. The average duration of HIV seropositivity was 13.7 years, and the average CD4+ count nadir was 350/mm³. Follow-up data for patients with multiple cytologies averaged 46 months. Among the findings, 58.9% of patients underwent high-risk HPV detection, with 63.0% testing positive for one or more high-risk HPV types. The results of cytologies were: 2.8% non-reportable; 41.8% normal; 32.4% ASCUS; 16.1% low-grade squamous intraepithelial lesion (LSIL); 5.5% high-grade squamous intraepithelial lesion (HSIL); 1.2% ASC-H. HSIL was observed in 10.4% of patients during screening. HRA results showed: 0.6% non-reportable; 0.9% proctitis; 76.3% normal; 13.9% condyloma; 3.8% AIN1; 1.9% AIN2; 1.9% AIN3; 0.6% anal squamous cell carcinoma (ASCC). Weak correlation existed between individual cytology grades and corresponding dysplasia grades on HRA ($\tau b=0.216$, $p<0.001$). However, abnormal cytology significantly increased the odds (10.219 times higher) of AIN+ findings on HRA compared to normal cytology. Specifically regarding ASCUS results, the analysis did not show a significant association between abnormal HRA and having one or more HR-HPV types (OR=0.286, p=0.289).

Conclusions: This study raises questions about the actual prevalence of AIN in the Belgian population, noting the notably low occurrence of AIN+ lesions in the Gent population of HIV-positive MSM. While the weak agreement between cytology and HRA underscores the complexity of screening methods, abnormal cytology emerged as a good indicator for AIN+ on HRA. Although this specific study couldn't definitively determine the diagnostic utility of an HR-HPV test in ASCUS results, literature emphasizes its value. ASCUS/HR-HPV-positive or ASCUS/HPV16/18-positive individuals had significantly higher risks of high-grade anal intraepithelial neoplasia (HGAIN) compared to ASCUS/HR-HPV-negative individuals, aligning with findings from research indicating higher HGAIN risks with HR-HPV and HPV16/18 positivity (Sambursky et al.).

BELGIAN SOCIETY OF NEUROGASTROENTEROLOGY AND MOTILITY (BSNM)

- N01 -

OPTIMAL DURATION OF THE STABILIZATION PERIOD DURING 3D HIGH-DEFINITION ANORECTAL MANOMETRY: INFLUENCE ON RESTING PRESSURES AND DETECTION OF OTHER EVENTS. N. Torres (1), F. Wuestenberghs (1) / [1] Centre Hospitalier Universitaire Mont-Godinne, Belgium, Gastro-entérologie.

Introduction: The London protocol sets a standardized way to perform anorectal manometry. However, this protocol is mainly based on expert opinion. Particularly, the IAPWG recommends a stabilization period, lasting from the beginning of the recording once the probe is in place to the beginning of the first voluntary squeeze, of 3 minutes. This period is considered the time necessary for the anal tone to return to its baseline value and for the patient to become familiar with the probe. Still, the data supporting this recommendation are lacking.
Aim: Our study aims to assess the optimal duration of the stabilization period by using a modified London protocol with longer stabilization times and to assess its consequences on the detection of other events. We hypothesized that 3 minutes of stabilization are insufficient and that, by extending the stabilization period, a certain number of events relevant to the diagnosis, and thus to the subsequent management of the patient, could be observed: spontaneous internal anal sphincter relaxations (SIASR), presence and disappearance of ultralow waves (USW), presence of spontaneous contractions of the rectum or recto-sphincter antagonism.
Methods: All consecutive 3D high-definition anorectal manometry tracings performed at a single centre (CHU UCL Namur, Godinne hospital) between February 2018 and September 2020 were analyzed retrospectively. All patients underwent investigation using the ManoScan AR 3DTM catheter (Given Imaging), performed by a physician, and those with a stabilization period of over 11 minutes were kept for analysis. The subjective timing for an optimal stabilization period was independently and blindly assessed by two investigators. The detection of manometric events during this period (mainly the presence of SIASR and USW) was also assessed. Demographic and manometric parameters were retrieved. The study was approved by the local ethics committee (CE number 191/2021).
Results: One hundred sixty-eight tracings were kept for analysis, with female predominance (72.0%). The main indications for manometries were the workups of constipation (42.8%) and faecal incontinence (35.1%). The mean subjective stabilization periods were 3.0 and 6.5 minutes according to the two investigators. Nearly half of USW at the beginning of the recording will disappear over time, on average after 4.7 minutes. The diagnosis of USW was reduced nearly by a third when waiting for 10 minutes of stabilization compared to 3 minutes. Peaks of frequency for SIASR are at 5-6 minutes and 8-10 minutes. The presence of SIASR would have been missed in three-quarters of the patients if the stabilization period had been limited to 3 minutes instead of 10. The ultraslow waves were mainly observed in constipated patients, while patients with faecal incontinence had more frequent SIASR. Extending the stabilization period up to 10 minutes is well accepted by the patients.
Conclusions: A stabilization period of 3-6 minutes seems sufficient to obtain stable resting pressures. However, extending the stabilization period is well accepted by patients, reduces overdiagnosis of USW and increases the detection rate of SIASR. Further studies are required to assess the stabilization period objectively and to determine if the detection of manometric events during the period are clinically relevant.

- N02 -

ACUTE FOOD INDUCED MUCOSAL ALTERATIONS VISUALIZED USING CONFOCAL LASER ENDOMICROSCOPY IN THE DUODENUM OF IRRITABLE BOWEL SYNDROME PATIENTS. L. Balsiger (1), K. Raymenants (1), J. Schol (1), L. Juvyns (1), K. Routhiaux (1), J. Tóth (1), R. Farré Marti (1), T. Vanuytsel (1), J. Tack (1) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, TARGID.

Introduction: Irritable bowel syndrome (IBS) is a common disorder of gut-brain interaction (DGBI). Many patients suffer from food related onset or increase of symptoms, possibly mediated through local allergic reactions. Confocal laser endomicroscopy (CLE) has previously shown acute food-triggered disruption of the duodenal epithelial barrier in IBS upon local food administration during the procedure. Upon exclusion of foods that triggered epithelial changes, patients reported symptomatic improvement.
Aim: The aim of the current study was to evaluate whether food induced alterations were present in IBS and whether these coincided with increased mucosal permeability and mast cell activation ex-vivo.
Methods: In Rome IV IBS patients (non-constipated), allergic sensitization to nutrients was excluded by specific serum immunoglobulin E (IgE) tests. CLE was performed during upper GI endoscopy after intravenous administration of 2.5 mL fluorescein 10%. Duodenal mucosa was visualized before and after sequential application of 10mL dissolved fish and shellfish, nuts, egg white, soy, milk lyophilizate and wheat – foods were administered in a randomized order. The procedure was stopped after visualization of an acute alteration. In line with previous literature, acute alterations were defined as acutely occurring fluorescence and particles in the duodenal lumen. Duodenal biopsies were obtained

after food exposures to measure trans-epithelial electrical resistance (TEER) in mini Ussing chambers as a marker of intestinal permeability. Values were compared to baseline biopsies obtained during a preceding gastroscopy. Tryptase was measured in biopsy supernatants after 24h incubation at baseline and after CLE. Tryptase values were normalized for biopsy weight. Data are reported as mean± SEM. Comparisons were done using two-sided paired t-tests. Results were considered significant if $p<0.05$.
Results: Data was available from 20 patients (90% female, age 34±3 years, BMI 23±1 kg/m2) that underwent a total of 32 CLE exams. In 9% (n=3) of exams, altered mucosa was present prior to any food administration. In the remaining 91% (n=29) acute alterations were observed after food exposure. The highest percentage of alterations was observed after milk administration (alterations were observed in 54% of exposures, 7 acute alterations / 13 total exposures to milk) followed by fish and shellfish (50%, 7/14), egg (36%, 5/14), nuts (33%, 5/15), wheat (30%, 3/10) and soy (20%, 2/10). Ex vivo, TEER was not significantly altered after acute mucosal reactions compared to baseline (26 ± 1 Ωcm² vs 25 ± 0.9 Ωcm², $p = 0.33$). Supernatants of biopsies taken after baseline and after food exposure did not differ in tryptase content (1.03±0.13 mcg/g vs 1.38±0.20, $p = 0.16$).
Conclusions: Using CLE, acute food induced alterations of the duodenal mucosa were visualized in a majority of non-constipated IBS patients in this study. Food induced alterations of the epithelial barrier did not result in acutely altered measures of permeability nor increased tryptase release ex vivo. The underlying mechanism of the observed CLE changes requires further investigation.

- N03 -

VARIATION IN GASTRODUODENAL FUNCTION TESTING IN CLINICAL PRACTICE: RESULTS FROM AN INTERNATIONAL SURVEY. S. Kindt (1), A. Fikree (2), M. Fox (3) / [1] UZ Brussel, Brussels, Belgium, Gastroenterology, [2] University College London Hospital, London, UK, London, United Kingdom, Gastroenterology, [3] University Hospital Zürich, Zürich, Switzerland, Clinic for Gastroenterology & Hepatology.

Introduction: When endoscopy and imaging fail to identify structural abnormalities, patients with digestive symptoms after meals may be referred for further evaluation of gastroduodenal function (GDF). Different techniques are available for this assessment.
Aim: This study aims to audit the availability of these techniques in practice and to compare the standard operating procedures (SOPs), data analysis and measurements.
Methods: Members from expert centres offering GDF testing indicated the patient load, the availability and desirability of 15 different testing modalities including non-invasive imaging (e.g. scintigraphy), manometry, and full thickness biopsies) for the assessment of gastric emptying, accommodation, sensitivity or motility. For available tests, multiple-choice questions assessed the indication for referral and details on SOPs including meal type.
Results: Twenty-two respondents from 12 different countries, seeing each on average 46 [24-61] patients with suspected gastroduodenal dysfunction per month, completed the audit. Gastric emptying scintigraphy (GES) was available to 86% of respondents, nutrient drinking challenge (NDC) 50%, EndoFLIP 46%, gastric emptying breath test (GEBT) 36%, intragastric pressure measurement (IGP) 32%, antroduodenal manometry (ADM) 32%, and body surface mapping (BSM) 32%. Less than 30% of participants had access to any of the other testing modalities. Gastric MRI (50%), BSM (32%) and IGP (27%) were most desired. Testing modalities were utilised for assessing nausea/vomiting (70%) and postprandial symptoms (58%) and less frequently for epigastric pain (31%). Meal composition, either solid or liquid, and symptom assessment differed widely for the same test as well as between modalities. When performing NDC, all respondents provided a standardised liquid test meal (100%) and always assessed pain and fullness (resp. 90% and 100%). However, during GES and GEBT, resp. 64% and 50% did not record symptoms. There was also large variation in meal volume, caloric content, test duration and reference values used for the individual tests.
Conclusions: Availability, indication, data acquisition and analysis of GDF testing vary between centres. Standardisation of test methodology, and SOPs including type of test meal is required to ensure generalisability of test interpretation, communication between different sites, further research and ultimately patient benefit.

- N04 -

NAVIGATING THE MAZE OF FUNCTIONAL DYSPEPSIA: EMERGENCE OF A NEW ENTITY, POSTPRANDIAL EPIGASTRIC PAIN. C. Van de Bruaene (1), F. Carbone (1), M. Jones (2), J. Tack (1) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Gastroenterology, Neurogastroenterology & Motility, [2] Macquarie University, North Ryde (New South Wales), Australia, Psychology, Macquarie University, North Ryde, New South Wales, Australia.

Introduction: Historically, functional dyspepsia (FD) has been subdivided into postprandial distress syndrome, PDS, with meal-related symptoms (i.e., early satiation, postprandial fullness) and epigastric pain syndrome, EPS, defined as meal-unrelated (i.e., epigastric pain and burning) according to the Rome criteria. However, currently available research has not addressed the extent to which epigastric pain is truly meal-unrelated.

Aim: To use two independent, prospectively collected FD databases to assess the relationship of epigastric pain to ingestion of a meal.
Methods: Two databases were used for this purpose. The first cohort consisted of 495 clinical FD patients in a tertiary setting, referred by gastroenterologists, who took a standard gastric emptying breath test meal, followed by simultaneous registration of perceived symptoms (i.e., pain, fullness…). Scores ranged 0-4 (with 0= absent and 4= unbearable). A score of 2 (i.e., bothersomeness threshold) was defined as clinically relevant for all symptoms. The second international and multicenter dataset consisted of 1080 DGBI (disorders of the gut-brain interaction) patients in 16 centers (9 European and 7 Asian), completing an extended Rome questionnaire, based on recall data, including meal-related questions. Patients who reported meal-related epigastric pain, meal-unrelated epigastric pain and postprandial distress syndrome symptoms were compared with respect to the prevalence of a range of symptoms, and demographic characteristics in both cohorts.
Results: The meal-related symptom assessment identified 318 (64.2%) clinical FD patients with postprandial distress (PDS) symptoms (i.e. bothersome fullness following meal intake). In patients not registering PDS symptoms (N= 175), a higher proportion, 13.1%, experienced postprandial epigastric pain (pEPS) compared to the 10.9% patients experiencing meal-unrelated epigastric pain (murEPS). When comparing the different patient categories (PDS, pEPS and murEPS respectively, according to symptom pattern) patients with pEPS had the tendency to experience more epigastric burning ($p= 0.089$), whereas PDS patients experienced more bloating ($p< 0.001$). Gastric emptying rates, both for liquids and solids, did not differ among categories. In the international study, 483/1080 DGBI patients fulfilled Rome IV FD criteria, with 181 pure PDS, 133 pure EPS and 169 overlap PDS/EPS. Of the pure EPS patients, 44 (33.1%) reported meal-related pain. In this cohort, heartburn was more frequently reported by murEPS patients (31.5%) compared to pEPS patients (22.7%), yet not statistically significant. In both datasets age and weight did not significantly differ across patient categories. However, in the international study, BMI was significantly higher in murEPS patients, compared to pEPS patients ($p= 0.035$). Also, a tendency for a higher BMI in murEPS patients was found in the first study ($p= 0.063$).
Conclusions: In contrast to earlier characterization of EPS symptoms as being meal-unrelated, two large independent datasets identify a substantial FD subgroup of patients with meal-related epigastric pain, which has the tendency to be more readily accompanied by epigastric burning and a lower BMI, compared to meal-unrelated epigastric burning. Further research is needed to better characterize these patients, the underlying pathophysiology, and the response to treatment options compared to meal-unrelated epigastric pain.

- N05 -

REDUCED MACRONUTRIENT AND FODMAP INTAKE IN IBS PATIENTS FOLLOWING THE LOW FODMAP DIET. K. Routhiaux (1), K. Van den Houte (1), L. Waegemans (1), J. Lee (2), J. Muir (3), J. Tack (1) / [1] KUL - University of Leuven, Leuven, Belgium, TARGID, [2] Monash University and Mount Sinai Medical Centre, New York, United States, Gastroenterology, Central Clinical School, [3] Monash University and Mount Sinai Medical Centre, New York, United States, Department of Gastroenterology, Central Clinical School.

Introduction: Irritable bowel syndrome (IBS) is a disorder characterized by abdominal pain related to bowel habits. A diet low in fermentable oligo- di- monosaccharides and polyols (FODMAPs) has shown efficacy in IBS. A blinded reintroduction revealed a personalized pattern of symptom recurrence and allows an objective identification of individual FODMAP triggers. However, the role of dietary macronutrient and FODMAP intake at baseline and the magnitude of changes during the diet in determining treatment success have not been established in detail.
Aim: To evaluate dietary macronutrient and FODMAP intake at baseline and during low FODMAP diet and their relationship to symptom severity in tertiary care IBS patients.
Methods: Seven-day food diaries were collected from tertiary care IBS patients during regular food intake and during the strict low FODMAP diet (LFD). Macronutrient analysis was performed using MyFitnessPal and FODMAP analysis was performed using the Monash FODMAP calculator. Individual FODMAP triggers were identified after a blinded reintroduction of individual FODMAP powders. Baseline FODMAP intake was compared in patients with and without these FODMAP triggers. In addition, patients filled out IBS-SSS questionnaires to score their symptoms. Data are reported as mean±SEM. Continuous variables were compared using t-tests, a p-value of ≤ 0.05 was considered significant. Correlation was evaluated by means of the Pearson correlation coefficient.
Results: Data from 69 IBS patients (84% female, age 35±2 years, BMI 24.7±0.7 kg/m²) treated with the low FODMAP diet were analysed for macronutrient analysis before and during the diet. Compared to baseline food intake, a significant decrease occurred in intake of calories (1732±53kcal vs. 1585±52kcal, $p< 0.001$), carbohydrates (197±7g vs. 182±7g, $p< 0.01$), sugar (52±4g vs. 42±3g, $p< 0.001$), fat (71±4g vs. 64±3g, $p< 0.05$) and saturated fat (22±1g vs 19±1, $p< 0.05$) during the LFD. Data from 46 patients was available for FODMAP analysis. Compared to baseline, a significant decrease was observed in the overall FODMAP intake (11.7±1.0g vs. 3.1±0.2g, $p< 0.0001$) after the LFD For the individual FODMAP intake, a significant decrease was found in excess fructose (1.7±0.3g vs. 0.7±0.05g, $p< 0.01$), lactose (6.1±1.0g vs. 0.8±0.2g, $p< 0.0001$), sorbitol (0.6±0.1g vs. 0.1±0.02g, $p= 0.0001$), mannitol (0.1±0.02g vs. 0.04±0.006g, $p< 0.01$), fructans (2.4±0.2g vs. 1.0±0.07g, $p< 0.0001$), and galacto-oligosaccharides (0.8±0.07g vs. 0.5±0.03g, $p< 0.001$) during the LFD , compared to baseline. The response rate (measured by IBS-SSS) was not correlated with caloric intake ($r = 0.2$), carbohydrates ($r = 0.02$), fat ($r = 0.06$) or total FODMAP intake ($r = 0.06$). According to the blinded reintroduction,

for a given FODMAP, baseline individual intake was not significantly higher in patients where this FODMAP triggered symptom recurrences compared to patients where this did not trigger symptoms.
Conclusions: These findings confirm a reduced intake of macronutrients (carbohydrates and fats) during the LFD, compared to regular food intake in IBS patients. In addition, a significant reduction was found in intake of total and individual FODMAPs during the LFD. No correlation was found between the response rate and the difference in macronutrients and FODMAP intake during the LFD, compared to regular food intake. Volume of specific FODMAP intake at baseline did not determine their ability to trigger symptoms upon blinded reintroduction.

- N06 -

CHANGES IN EDN LEVELS AFTER FOLLOWING A DIET OR MEDICAL THERAPY. C. Reulens (1), J. Toth (1), K. Routhiaux (1), K. Van den Houte (1), F. Carbone (1), J. Tack (1) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Chronic Diseases and Metabolism.

Introduction: Irritable bowel syndrome (IBS) affects about 10 to 15% of the global population. Based on the dominant stool form, it can be subdivided into diarrhea-predominant (IBS-D), constipation-predominant (IBS-C), mixed type IBS (IBS-M) or unclassified IBS (IBS-U). Patients report recurrent abdominal pain and other symptoms as bloating, abdominal distention and flatulence. In the DOMINO study, a FODMAP lowering diet application (DOMINO app) showed a higher responder rate compared to standard medication (otilonium bromide, OB) in 472 primary care IBS patients. The pathophysiology of IBS is multifactorial, but recent research is focusing on low-grade inflammation. An increased number of eosinophils has been reported in the mucosa of IBS patients compared to healthy controls. Moreover, faecal eosinophil-derived neurotoxin (EDN) levels are elevated in IBS compared to controls (Casado-Bedmar 2022).
Aim: We aimed to analyse the faecal EDN levels in stool samples of IBS-D primary care patients from the DOMINO cohort and their evolution after a FODMAP lowering diet or OB treatment.
Methods: IBS and its subtype were clinically diagnosed by primary care physicians at baseline. Patients collected a stool sample before and after an 8 week treatment period with either the DOMINO diet or OB. Patients filled out a Bristol stool scale form when collecting the stool sample. Faecal EDN levels are measured in stool samples of IBS-D patients before and after treatment by an ELISA assay (Diagnostics Development AB, Uppsala, Sweden). In addition, demographic data was collected and patients filled out questionnaires regarding their symptoms (IBS-SSS). EDN levels were compared at baseline and after treatment. Data was analysed by non-parametric t-tests and a p-value <0.05 was considered significant.
Results: Stool samples of 120 IBS-D patients (69,2 % female, mean age 37 ± 14) were analysed. BMI or the stool form according to the Bristol Stool Form Scale were not associated with EDN levels before or after treatment. EDN levels were not correlated with IBS-SSS scores. We found no significant difference in EDN levels before and after treatment with OB (n = 60, 69,6 ± 12,0 µg/g vs. 66,8 ± 9,7 µg/g , p = 0.92) or the FODMAP lowering diet (n = 60, 126,8 ± 28,5 µg/g vs. 77,9 ± 11,5 µg/g, p = 0.06). However, there was a significant difference in EDN levels in men (n = 37, 100,6 ± 22,6 µg/g vs. 48,5 ± 9,0 µg/g, p = 0.005) but not in women (n = 83, 96,8 ± 20,2 µg/g vs. 83,1 ± 9,9 µg/g, p = 0.59) after treatment. A numerical decrease in EDN levels in men was observed with both the DOMINO diet and with OB treatment but reached statistical significance only in the former (respectively n = 18, 114,5 ± 34,4 µg/g vs. 50,5 ± 12,6 µg/g, p = 0.03 and n = 19, 86,7 ± 29,9 µg/g vs. 46,3 ± 13,3 µg/g, p = 0.07).
Conclusions: In IBS-D patients as a group, EDN levels and their evolution were not correlated to symptom severity or symptom improvement after following an 8 week treatment with either diet or medication. In male patients, treatment response was associated with a decrease in EDN compared to females after the DOMINO diet. The role of eosinophils in treatment response in IBS subgroups deserves further in-depth studies.

- N07 -

THE EFFECTIVENESS OF PROTON PUMP INHIBITORS PRIMARILY IN THE TREATMENT OF PATIENTS WITH ACID-DEPENDENT GASTROESOPHAGEAL DISEASES DEPENDS ON THE BASAL SECRETION OF HYDROCHLORIC ACID. I. Paliy (1), S. Zaika (2), K. Ksenchyna (1) / [1] National Pirogov memorial medical university, Vinnytsya, Ukraine, Department of internal and family medicine, [2] National Pirogov memorial medical university, Vinnytsya, Ukraine, Department of internal and family medicine.

Introduction: The resistance of Helicobacter pylori (H.p.) to eradication therapy schemes is relevant for modern gastroenterology. One of the ways to overcome this problem is to achieve sufficient blocking of HCl secretion in the stomach. However, in not all patients with acid-dependent gastroesophageal diseases, we can achieve blockade of gastric HCl secretion using standard doses of proton pump inhibitors (PPIs). Thus, it becomes relevant to develop criteria for predicting the effectiveness of PPIs before the eradication of H.p.
Aim: Based on the data of daily gastro-pH monitoring, evaluate the effectiveness of PPI on the first day of treatment depending on the basal secretion of HCl.

Methods: We analyzed 83 results of daily gastro-pH monitoring on the first day of taking PPIs in patients with acid-dependent gastroesophageal diseases. The separation criterion was the indicators of express gastro-pH monitoring (X pH >2.48 units, Me pH >2.3 units and Mo pH >2.35 units), which we established in previous studies. Express gastro-pH monitoring was performed for all patients before daily gastro-pH monitoring. The patients were divided into two groups: 55 patients in whom the indicators of express gastro-pH monitoring were less than the suggested ones (group I) and 28 patients in whom the indicators of express gastro-pH monitoring corresponded to the proposed criteria (group II). Both groups were comparable in terms of age, sex, height, body weight, and prescribed PPI, which allowed a comparative assessment between groups. We studied indicators of intragastric pH (X pH, Me pH, and Mo pH) of daily gastro-pH monitoring for the following time periods: 1 Basal period - time from the start of daily gastro-pH monitoring to the reception of the first PPI dose (1 hour); 2. Time after taking the first PPI dose until the end of monitoring (23 h); 3. Night time period (22:00 - 07:00).
Results: Analyzing intragastric pH indicators during the basal period, it was found that in patients of the I group, the indicators of X pH, Me pH and Mo pH were significantly lower ($p<0.01$) than in patients of the II group and, accordingly, were (1.9±0.09 , 1.75±0.07, 1.68±0.07 vs. 2.2±0.09, 2.03±0.1, 1.96±0.1). 23 hours after taking the first dose of PPI in patients of group I, the indicators of intragastric pH were significantly lower ($p<0.01$) than in patients of group II and were, respectively, (4.2±0.2, 4.07±0.2 , 3.6±0.2 vs. 4.9±0.2, 4.9±0.3, 4.5±0.3). Similar results were obtained by us during the analysis of the night time period. It was established that in the I group, the indicators of intragastric pH during the night time period were significantly lower ($p<0.01$) than in the patients of the II group and, accordingly, were (4.3±0.2, 4.2±0.3, 3, 9±0.3 vs. 5.03±0.2, 5.02±0.3, 4.9±0.4).
Conclusions: 1. Basal gastric acidity affects the effectiveness of the acid-blocking action of PPIs on the first day of treatment both during the 23-hour period and during the night period. 2. The proposed criteria of express gastro-pH monitoring for prognostic assessment of the acid-blocking effect of PPIs before the start of treatment are sufficient.

- N08 -

CLINICAL AND PSYCHOSOCIAL CHARACTERISTICS OF ADULT PRIMARY CARE IBS PATIENTS IN BELGIUM: A CROSS-SECTIONAL POST HOC ANALYSIS OF THE DOMINO STUDY. R. Wils (1), B. Broeders (1), K. Van den Houte (1), F. Carbone (1), J. Tack (1) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Gastroenterology.

Introduction: Irritable bowel syndrome (IBS) is a common functional gastro-intestinal disorder associated with a decreased quality of life, substantial socioeconomic consequences and a considerable psychological burden. The majority of IBS patients are diagnosed and managed in primary care, but this setting is underinvestigated to date.
Aim: The present study aimed to improve our understanding of IBS in primary care by evaluating the clinical and psychosocial characteristics of adult primary care patients with the disorder.
Methods: We performed a cross-sectional post hoc analysis of the DOMINO trial, which yielded a large Belgian cohort of 483 primary care patients, newly diagnosed with and treated for IBS by 69 general practitioners. We investigated baseline demographics and questionnaires assessing Rome IV IBS criteria and stool pattern subtype, symptom severity (IBS-SSS), quality of life (IBS-QoL), somatisation (PHQ-12), depression (PHQ-9) and anxiety (GAD-7). Differences according to IBS Rome IV subtype and IBS Rome IV positivity (Rome+ vs. Rome-) were studied by the Mann-Whitney, Kruskal-Wallis, Fisher's Exact and Chi-square test. Furthermore, statistically significant predictors of IBS-SSS and IBS-QoL were identified by multiple linear regressions and general linear models. Data are shown as mean±standard deviation.
Results: 70.4% of the primary care IBS patients (n=483, 41±14.8 years, 76% female) fulfilled the Rome IV criteria (Rome+, n=317). The stool pattern subtype distribution according to the Rome IV diagnostic questionnaire (n=450) was: 20.2% constipation (IBS-C), 33.3% diarrhea (IBS-D), 30.9% mixed (IBS-M) and 15.6% unclassified (IBS-U). Mean IBS-SSS (n=453) was 267.6±97.8 with 45.5% and 36.4% of the cases considered as moderate and severe respectively. Of the patients not fulfilling Rome IV (n=133), 43.6% did not meet the criteria based on frequency of abdominal pain. The Rome+ group was younger (38.5±13.8 vs. 46.8±14.8 years, $p<0.001$) and more likely to be female (79.8% vs. 65.4%, $p=0.002$) compared to Rome-. The prevalence of IBS-D and IBS-M was significantly lower (25.6% vs. 36.6% and 19.5% vs. 35.6% respectively, $p<0.05$) and IBS-U was higher (33.8% vs. 7.9%, $p<0.05$) in the Rome- group. Rome- patients had a lower IBS-SSS (201.5±99.8 vs. 295.4±82.9, $p<0.001$), a better quality of life (IBS-QoL 23.4±14.3 vs. 35.4±16.9, $p<0.001$) and a lower psychosocial comorbidity compared to Rome+ (PHQ-12 7.0±3.9 vs. 9.2±4.5, $p<0.001$; PHQ-9 5.8±4.6 vs. 7.4±5.1, $p=0.001$ and GAD-7 5.3±4.5 vs. 7.2±5.1, $p<0.001$). IBS-U patients were significantly older than IBS-M and IBS-D patients (47.3±13.6 vs. 37.3±13.4 and 39.9±14.6 years respectively, $p<0.001$) and IBS-C patients were significantly older than IBS-M participants (43.4±15.1 vs. 37.3±13.4 years, $p=0.002$). The male proportion was significantly higher in IBS-U than in IBS-C and IBS-M (42.9% vs. 16.5% and 15.8% respectively, $p<0.05$). IBS-U participants had a significantly lower IBS-SSS compared to IBS-M, IBS-D and IBS-C (203.3±104.2 vs. 294.8±92.3, 265.0±89.2 and 280.0±93.9, $p<0.001$, $p=0.001$ and $p<0.001$ respectively). IBS-M had a higher IBS-SSS compared to IBS-D (294.8±92.3 vs. 265.0±89.2, $p=0.03$). IBS-U patients reported a better quality of life compared to IBS-M, IBS-D and IBS-C (IBS-QoL 22.9±14.1 vs. 37.1±17.7, 31.6±16.0 and 31.1±17.0, $p<0.001$, $p=0.003$ and $p=0.02$ respectively).

IBS-U and IBS-D patients scored significantly lower on the PHQ-12 compared to IBS-M (7.3±4.6 and 8.2±4.2 vs. 9.6±4.4, p=0.001 and p=0.04 respectively). In addition, IBS-U had lower depression and anxiety levels compared to IBS-M (PHQ-9 5.6±5.0 vs. 7.7±5.1, p=0.005 and GAD-7 5.4±4.7 vs. 7.6±5.2, p=0.007). We identified age (p=0.001), PHQ-12 (p<0.001) and Rome subtype (p<0.001) as statistically significant predictors of IBS-SSS. PHQ-9 (p=0.003), GAD-7 (p=0.03) and IBS-SSS (p<0.001) were significant predictors of IBS-QoL.

Conclusions: In a large primary care IBS cohort, the majority of patients fulfilled the Rome IV criteria and were subtyped as IBS-D and IBS-M. Most patients were characterized by moderate or severe IBS-SSS. IBS-U and Rome-participants had a lower symptom severity, a higher quality of life and a milder psychological burden.

BELGIAN GROUP FOR DIGESTIVE ONCOLOGY (BGDO)

- O01 -

IMPACT OF [18F]ALF-NOTA-OCTREOTIDE PET/CT ON THE THERAPEUTIC MANAGEMENT OF NEURO-ENDOCRINE TUMOR PATIENTS. H. Leupe (1), E. Pauwels (1), T. Vandamme (2), W. Lybaert (3), B. Van den Broeck (4), C. Verslype (5), J. Jaekers (6), F. Van Herpe (5), J. Hofland (7), F. Cleeren (8), A. Brouwers (9), G. Bormans (8), M. Koole (10), E. Van Cutsem (5), K. Geboes (11), A. Laenen (12), J. Dekervel (5), S. Stroobants (13), C. Deroose (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Nuclear Medicine, [2] Universiteit Antwerpen / Antwerp University Hospital, WILRIJK (Antwerpen), Belgium, Oncology, [3] NETwerk Antwerpen-Waasland CoE, Edegem, Belgium, Oncology, [4] Ghent University Hospital, Ghent, Belgium, Nuclear Medicine, [5] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Digestive Oncology, [6] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Visceral Surgery, [7] Erasmus MC, University Medical Center Rotterdam, The Netherlands, Department of Internal Medicine, Section of Endocrinology, [8] KUL - University of Leuven, Leuven, Belgium, Radiopharmaceutical Research, [9] University Medical Center Groningen, Groningen, The Netherlands, Nuclear Medicine and Molecular Imaging, [10] KUL - University of Leuven, Leuven, Belgium, Nuclear Medicine and Molecular Imaging, Department of Imaging and Pathology, [11] Ghent University Hospital, Ghent, Belgium, Digestive Oncology, [12] KUL - University of Leuven, Leuven, Belgium, Biostatistics and Statistical Bioinformatics Center, [13] University hospital of Antwerp, Edegem, Belgium, Nuclear Medicine.

Introduction: Gallium-68 labelled somatostatin analogue ([68Ga]Ga-DOTA-SSA) PET/CT is the current gold standard for molecular imaging of the somatostatin receptor (SST) in neuroendocrine tumors (NETs). However, its widespread implementation in clinical practice is limited by practical and economic issues. [18F]AlF-NOTA-octreotide ([18F]AlF-OC) PET/CT offers several advantages to overcome these issues and is a promising alternative for [68Ga]Ga-DOTA-SSA PET/CT.
Aim: Our aim is to assess changes in TNM staging and differences in patient management when using [18F]AlF-OC PET/CT instead of [68Ga]Ga-DOTA-SSA PET/CT in the work-up of NET patients.
Methods: This study is a secondary endpoint analysis of our previously published multicenter study (Pauwels et al., J Nucl Med. 2023;64(4):632-638), which compared lesion detection between [18F]AlF-OC and [68Ga]Ga-DOTA-SSA PET/CT in NET patients. TNM staging was determined and compared for both tracers. For each patient, the blinded [68Ga]Ga-DOTA-SSA or [18F]AlF-OC PET/CT images were presented in random order at a multidisciplinary tumor board, consisting of at least two clinical NET experts, a surgeon and a nuclear medicine physician. The images were presented together with clinical information and compared with previous SSTR and [18F]FDG PET/CT imaging. After a consensus decision for patient management was recorded, the board was presented with the PET/CT images from the other SST tracer and a decision was made for the second tracer. Differences in management were classified as major if it entailed an intermodality change and minor if it led to an intramodality change.
Results: All 75 patients from the multicenter study were included for analysis. In total, the use of [18F]AlF-OC PET/CT led to differences in TNM staging and/or differences in clinical management in 16/75 patients. Compared with [68Ga]Ga-DOTA-SSA, the use of [18F]AlF-OC led to TNM staging changes in 10/75 patients (13.3%; downstaging in 3/10, upstaging in 7/10). In total, [18F]AlF-OC PET/CT impacted clinical management in 10/75 patients (13.3%), leading to a major difference in 7/10 cases (follow up for 7/7 patients based on [68Ga]Ga-DOTA-SSA PET/CT vs. switch to PRRT for five; switch to everolimus for one and start SSA for one patient based on [18F]AlF-OC PET/CT) and a minor change in 3/10 cases (follow-up for [68Ga]Ga-DOTA-SSA PET/CT vs. SSA dose escalation for [18F]AlF-OC). All ten cases with a difference in patient management between both PET tracers were caused by additional lesion detection by [18F]AlF-OC.
Conclusions: The use of [18F]AlF-OC resulted in TNM changes in a small minority of the patients (13.3%). Differences in clinical management were seen in 10 patients (13.3%), which were all cases of therapy intensification driven by higher number of lesions detected by [18F]AlF-OC PET/CT. The use of [18F]AlF-OC did not impact TNM staging or clinical management in the large majority of the patients (86.7%), further validating the potential for routine clinical use of [18F]AlF-OC PET/CT instead of [68Ga]Ga-DOTA-SSA PET/CT.

- O02 -

SEQUENTIAL EVEROLIMUS AND SUNITINIB TREATMENT IN METASTATIC PANCREATIC NEURO-ENDOCRINE NEOPLASMS AFTER FAILURE OF PREVIOUS TREATMENTS. O. Islam (1), G. Van de Vyver (2), C. Verslype (3), I. Borbath (4), J. Decaestecker (5), T. Botelberge (6), K. Geboes (7), P. Cuyle (8), M. Clausse (9), C. George (10), M. Polus (11), J. Coche (12), J. Van Laethem (13), W. Demey (14), A. Bols (15), G. Demolin (16), L. D'Hondt (17), M. Simoens (18), S. Chhajlani (19), I. Van der Massen (20), L. Mariën (20), W. Lybaert (21), M. Peeters (22), T. Vandamme (22) / [1] NETwerk Antwerpen-Waasland CoE, Edegem, Belgium, Medical oncology, [2] NETwerk Antwerpen-Waasland CoE, Edegem, Belgium, Gastro-Enterology, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Digestive Oncology, [4] UCL Saint Luc, Brussels, Belgium, Digestive Oncology, [5] AZ Delta,

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Introduction: Pancreatic neuroendocrine neoplasms (pNENs) account for 1-2% of all pancreatic neoplasms, with an incidence of 0.48/100,000 person years. The PI3K/Akt/mTOR pathway plays a pivotal role by regulating cell growth, proliferation, survival and protein synthesis in pNENs. The mTOR inhibitor Everolimus demonstrated a 65% risk reduction for progression compared to placebo and showed a prolongation of median progression-free survival (mPFS) from 4.6 to 11 months in the RADIANT-3 trial. Vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF) drive angiogenesis in pNENs, contributing to tumour development. Therefore, Sunitinib, a pan-tyrosine kinase inhibitor targeting the VEGF receptor, was developed as a treatment modality for pNENs. The SUN1111 phase-III study, showed a difference in mPFS between the treated group and the placebo group of 5.9 months (11.4 vs. 5.5 months), and an ORR of 9.3% versus 0% was established, respectively. Therefore both these compounds are used in the treatment of unresectable, metastatic, progressive, well-differentiated pNENs (or pNETS). Currently, patients often receive both treatments consecutively, but to date there is no consensus on the sequence in which both therapies should be given.
Aim: We set up a retrospective study using prospectively-collected data from the Belgian DNET database (a national database of 24 Belgian hospitals from the Belgian Group of Digestive Oncology, data collected since 2000) and Oncobase (a database of NETwerk, ENETS Centre of Excellence in Antwerp, data collected since 2017). To analyze the impact of the order of Everolimus and Sunitinib on overall surivival (OS) and median progression-free survival (mPFS1 and mPFS2), and describe the adverse events reported for both therapies . mPFS1 is the time from start first targeted therapy to progression under or end of this therapy and mPFS2, the time from start first targeted therapy to progression under or end of second targeted therapy in pNET patients.
Methods: Clinicopathological data from all metastatic G1, G2 and G3 pNET patients who received either Everolimus as second-line, followed by Sunitinib upon discontinuation (EverSun group) or the other way around (SunEver group), were collected. Follow-up time ranged from start of second line therapy until death or lost-to follow-up. Continuous data are described using means and standard deviation and compared using independent t-tests or ANOVA. Categorical data are described as counts and percentages and compared using Chi-square tests. Kaplan-Meier method is used for OS analysis and hazard ratio's, 95% confidence intervals are estimated using a Cox proportional hazards model and compared using Wald statistics. A two-sided p-value <0.05 is considered significant. Data analysis was performed using R. The study was conducted according to the Declaration of Helsinki and Good Clinical Practice guidelines.
Results: Our study population consists of 70 pNET patients, of which 46 male and 24 female. The Eversun group consists of 42 patients and the SunEver of 28 patients. Age at diagnosis ranges from 18 to 79. For all but 8 patients, WHO grade was reported, with 12 in the G1, 42 in the G2 and 8 in the G3 group. In the EverSun group median OS was 41.9m (95% CI; 25.6-64.2m) compared to 70.7m (95% CI; 47.3-82.7m) in the SunEver group. For the Eversun group mPFS1 was 8.2m (95% CI; 2.4-10.3m) and mPFS2 was 19m (95% CI; NA). For SunEver mPFS1 was 12.3m (95% CI; 4.9-16.2m) and mPFS2 was 32.3m (95% CI; 25.8-47.1m). Adverse events needing a dose reduction were mentioned 12 times for Everolimus (9 in EverSun and 3 in SunEver group) and 11 times for Sunitinib (8 in EverSun and 3 in SunEver group).
Conclusions: Our retrospective study provides more insights into the sequential treatment with Everolimus and Sunitinib demonstrating no statistical significant difference between the mPFS within the two treatment groups. Hence proving both modalities seem to be equal to each other in both sequences. However we do see a mOS difference of 28.8 months, suggesting some differences between the groups. For better understanding further analysis of the different grades and AEs are planned and prospective studies should be set up.

- O03 -

QUALI-NET: A PROSPECTIVE QUALITY OF LIFE STUDY ON PATIENT-REPORTED OUTCOMES IN NEURO-ENDOCRINE NEOPLASMS. O. Islam (1), L. Depauw (2), I. Van der Massen (3), L. Mariën (3), S. Chhajlani (2), C. De Weerdt (3), M. Simoens (4), D. Galdermans (5), W. Demey (6), T. Botelberge (7), M. Ulenaers (8), T. Rondou (8), W. Lybaert (9), M. Peeters (10), T. Vandamme (10) / [1] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Oncology, [2] UZA - NETwerk, Edegem, Belgium, Medical oncology, [3] UZA - NETwerk, Edegem, Belgium, NETwerk, [4] NETwerk, ZNA, Antwerpen, Belgium, Digestive Oncology, [5] NETwerk, ZNA, Antwerpen, Belgium, Thorax Oncology, [6] NETwerk, AZ KLINA, Brasschaat, Belgium, Digestive Oncology, [7] NETwerk, GZA, Antwerpen, Belgium, Digestive Oncology, [8] NETwerk, AZ Rivierenland Rumst/Bornem, Rumst, Belgium, Digestive Oncology,

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Introduction: Neuroendocrine neoplasms (NENs) are a rare type of tumour with rising incidence in the last couple of years. They are heterogeneous in biological characteristics, such as proliferation, differentiation, grade and possibility of hormone production. Histomorphologically we subdivide the group in well-differentiated neuroendocrine tumors (NETs) and poorly-differentiated neuroendocrine carcinoma's (NECs). The gastro-enteropancreatic (GEP) NENs are classified according to the WHO classification based on their proliferation and morphology, distinguishing grades 1, 2 and 3 NET and NEC. LungNEN are classified as well-differentiated typical and atypical carcinoids (TC and AC) and poorly-differentiated large cell or small cell NEC (LCNEC and SCNEC). Functional tumors are hormone producing. These low grade, slow growing tumors can lead to a prolonged disease course as patients have a long survival. Hence, attention to quality of life (QoL) in short- and long-term is important. Several studies on QoL of NEN patients have been conducted, mostly in small populations and for short periods. However, long term QoL data including all different disease subgroups is currently lacking.
Aim: We have set up a prospective 5-year study, assessing QoL through six-monthly questionnaires, identifying determinants of deterioration of all NEN patients within the centers of NETwerk, ENETS Center of Excellence in Antwerp. Leading to adaptations, in our care system, to the needs of the patient.
Methods: All NEN patients followed within NETwerk are included in the long-term prospective QoL study. This is measured through patient-reported outcome measures (PROMs), including a primary satisfaction survey at baseline and six-monthly questionnaires using the EORTC QLQ-C30 and EORTC QLQ-GI.NET21 questionnaires, during a period of 5 years. The questionnaire is sent out by e-mail, or on paper for those who do not use/have an e-mail address. Scores are recalculated to a 100-point scale. Data is collected through REDCap and linked to clinicopathological data in Oncobase (database of NETwerk, where data is collected since 2017). Data analysis is performed using R. Continuous data is described using means and standard deviation for baseline analysis. Comparison between two groups is performed using independent t-tests and between more than two groups using ANOVA. Linear mixed model is used for longitudinal data. A p-value less than 0.05 is considered significant. The study is conducted in accordance with the Declaration of Helsinki and the International Conference on Harmonization Good Clinical Practice Guidelines.
Results: So far we have included 162 patients of whom 92 males and 70 females. 93 subjects completed a second, 59 a third, 44 a fourth and 9 a fifth questionnaire. Baseline analysis has been done of 118 entries, which shows 9 unknown primaries, 7 lung, 3 esophageal, 47 small-intestine, 40 pancreaticoduodenal, 5 colon, 7 appendix. Of these, 93 patients have a non-functioning tumor while 3 had a gastrinoma, 3 had an insulinoma, 11 had carcinoid syndrome, and others are unknown. Within this population 5 patients had a MEN1 syndrome. Differences between GEPNEN and LungNEN are seen in physical function scores (75±25 vs 89±7), role functioning (68±32 vs 92±14) and emotional functioning (70±25 vs 86±13), respective p-values of 0.013, 0.015, and 0.067. No significant differences were found on other QoL domains. For functional (n=17) vs. non-functional (n=93) neoplasms, differences in emotion functional score (70±25 vs 78±17) and fatigue (41±30 vs 44±18) are seen, p-values of 0.032 and 0.037, respectively. Within the GEPNEN group comparison of pancreatic and extrapancreatic did not withhold any significant differences.
Conclusions: Between LungNEN and GEPNEN, QoL differences are seen on physical and role functioning, being better within the LungNEN patients. Functional tumors tend to score worse on QoL. As inclusion is still ongoing, further analysis is pending.

- O04 -

THE RELATION BETWEEN OVERALL SURVIVAL AND RECURRENCE-FREE SURVIVAL IDENTIFIES DIFFERENT METASTATIC BEHAVIORS IN PATIENTS OPERATED FOR COLORECTAL LIVER METASTASES.

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Introduction: In patients with liver-only colorectal liver metastases (CRLM), the benefit of surgery is generally attributed to its capacity to be curative. Accordingly, the recurrence-free survival (RFS) is considered as a reliable surrogate of the overall survival (OS) in these patients.
Aim: To verify this concept, we analyzed the correlation between RFS and OS in a series of patients operated for CRLM.
Methods: A series of 500 patients operated with a curative-intent for CRLM was reviewed. Primary tumor and CRLM clinicopathological characteristics, operative data and postoperative OS and RFS were analyzed. The correlation between RFS and OS was evaluated with Spearman's test.
Results: In the entire series, 5-year OS and RFS were 41.5% and 14.5%, respectively. In multivariate analysis, poorer OS and RFS were associated with T3-4 primary tumor and multiple CRLM and with multiple CRLM, respectively. In the whole cohort, RFS and OS were significantly correlated ($p<0.001$). According to the relation between RFS and OS, we identified 3 subgroups: 1) Patients (N=263) with a RFS≤2 years correlated with a OS≤5 years ($p<0.001$), 2) Patients

(N=175) with a RFS>2 years correlated with a OS>5 years (p<0.001) (N=175) and 3) Patients (N=62) with a RFS≤2 years not correlated with a OS>5 years (p=0.1). None of the traditional risk factors related to primary tumor, CRLM or operative characteristics was different between these 3 groups. In patients with a RFS≤2 years, only the possibility for reintervention was predictive for an OS>5 years.
Conclusions: The RFS and OS are not homogeneously correlated in patients who underwent surgery for CRLM. Therefore, RFS should not be systematically used as a surrogate of OS and as an indicator of the benefit of surgery in these cases. A subgroup of patients with slowly progressive disease could have a prolonged postoperative OS despite short RFS, suggesting that, in some cases, surgery could contribute to control rather than to eradicate the disease. The identification of predictive markers of such oligo/argo-metastatic behavior could potentially define new therapeutic attitudes in these patients.

- O05 -

INTERNATIONAL REAL-WORLD STUDY OF TOTAL NEOADJUVANT THERAPY (TNT) FOR LOCALLY ADVANCED RECTAL CANCER (LARC). A. Audisio (1), Leuven Rectal Cancer Group (2), A. Vanden Bulcke (3), M. Van Den Eynde (4), A. Dermine (5), F. Puleo (6), M. Diaz (7), Q. Gilliaux (8), A. Deleporte (9), K. Geboes (10), P. Martinive (11), T. Vandamme (12), A. Hendlisz (13), J. van Laethem (13), F. Sclafani (1) / [1] Hôpital Universitaire de Bruxelles, Bruxelles, Belgium, Depertment of Gastrointestinal Oncology, [2] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Digestive Oncology, Dept of Oncology, KU Leuven, [3] AZ Groeninge, Kortrijk, Belgium, Department of Gastroenterology, [4] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'oncologie médicale et de gastro-entérologie, [5] Centre Hospitalier de Jolimont-Lobbes., La Louvière, Belgium, Department of Gastrointestinal Oncology, [6] Chirec delta, Auderghem , Belgium, Department of Gastroenterology, [7] CHU Ambroise Paré MONS, Mons, Belgium, Department of Gastroenterology, [8] Université catholique de Louvain, CHU UCL Namur, Yvoir, Belgium, Department of Gastrointestinal Oncology, [9] CHU Saint-Pierre, Brussels, Belgium, Department of Gastrointestinal Oncology, [10] Universitair ziekenhuis Gent, Belgium, Department of Gastrointestinal Oncology, [11] Institut Jules Bordet, Brussels, Belgium, Department of Radiotherapy, [12] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Department of Gastrointestinal Oncology, [13] Hôpital Universitaire de Bruxelles, Bruxelles, Belgium, Department of Gastrointestinal Oncology.

Introduction: TNT has recently emerged as a standard treatment for LARC, showing superiority over conventional neoadjuvant chemoradiotherapy. However, use and outcome of the different TNT regimens in real-world practice are largely unknown.
Aim: The aim of this study is to describe real-word practice, safety and efficacy of TNT for LARC in a large international series.
Methods: This is an international, multicentre, retrospective study sponsored by the Institut Jules Bordet. Eligibility was limited to newly diagnosed LARC patients treated with TNT between March 2013 and May 2023 and outside the context of a clinical trial. Data were collected into a central electronic database, and remotely monitored. Descriptive statistics were used, and survival outcomes were estimated with Kaplan-Meier curves.
Results: 1,272 eligible patients were included from 47 centres (10 of which from Belgium) across four continents (Europe, Asia, North America and South America). Baseline characteristics were as follows: 63% males, median age 60 years (range 21-88), 47% low rectum, 26% cT4, 47% cN2, 49% EMVI+, 59% CRM+. In the overall population, 21% of the resected patients had a pathological complete response (pCR), while 11.3% were managed according to a watch-&-wait (w&w) strategy. Median follow-up was 24.1 months (IQR 23.7). Local and distant recurrences after curative-intent surgery occurred in 5.5% and 16.2% of patients, respectively. 3-year event-free survival (EFS) was 68.3%, while 3-year overall survival (OS) was 89%. Serious adverse events were reported in 4.3% of patients during radiotherapy, and in 14.7% during chemotherapy. TNT strategies included: short-course radiotherapy followed by consolidation chemotherapy (SCRT-CNCT, 34.5%), induction chemotherapy followed by chemoradiotherapy (INCT-CRT, 30.5%), induction chemotherapy followed by chemoradiotherapy and consolidation chemotherapy (INCT-CRT-CNCT, 17.4%), chemoradiotherapy followed by consolidation chemotherapy (CRT-CNCT, 15%), and induction chemotherapy followed by short-course radiotherapy (INCT-SCRT, 2.6%). Rates of pCR, w&w, local recurrence, distance recurrence, 3-year EFS and 3-year OS by TNT strategy were: 23%, 11.6%, 5.6%, 12.3%, 66.1% and 89.5%, respectively, for SCRT-CNCT; 21%, 5.1%, 5%, 13.8%, 71.8% and 90.5%, respectively, for INCT-CRT; 18%, 8.6%, 5.6%, 20.9%, 72.6%, and 86.4%, respectively, for INCT-CRT-CNCT; 20%, 27.2%, 5.6%, 21.6%, 59.8% and 89.7%, respectively, for CRT-CNCT; 26%, 6.1%, 11.1%, 22.2%, 62%, 88.6%, respectively, for INCT-SCRT. TNT regimens included: RAPIDO (45.4%), PRODIGE-23 (21.9%), OPRA with CNCT (18.7%), and OPRA with INCT (14%). Rates of pCR, w&w, local recurrence, distance recurrence, 3-year EFS and 3-year OS by TNT regimen were: 23%, 11.7%, 5.6%, 12.1%, 66.3%, and 89.6%, respectively, for RAPIDO; 22.3%, 5.2%, 2.8%, 14.9%, 75.1%, and 93.5%, respectively, for PRODIGE-23; 20%, 25%, 5.7%, 22.1%, 60.8%, and 89.1%, respectively, for OPRA-CNCT; 18.3%, 4.5%, 6.8%, 11%, 62.6% and 89.2%, respectively, for OPRA-INCT.
Conclusions: This is the largest real-world study of TNT for LARC. Our findings show substantial variation in the choice of TNT sequence and regimen. Efficacy and safety results are overall in line with those reported in clinical trials,

and confirm feasibility of TNT in a real-world setting. Patient recruitment is ongoing, and updated results with propensity score matching analyses will be reported at the meeting.

- O06 -

IMMUNO-MOLECULAR MODULATION IN PANCREATIC CANCER FOLLOWING ISOTOXIC HIGH-DOSE STEREOTACTIC BODY RADIOTHERAPY (IHD-SBRT). C. Bouchart (1), O. Azurmendi Senar (2), J. Navez (3), L. Verset (4), A. Boisson (5), M. Hein (6), N. D'Haene (7), D. Van Gestel (8), L. Moretti (8), P. Demetter (9), J. Bachet (10), K. Willard-Gallo (5), R. Nicolle (11), T. Arsenijevic (2), J.-L. Van Laethem (12) / [1] Institut Jules Bordet, Brussels, Belgium, Radiotherapy-Oncology, [2] ULB, Brussels, Belgium, Laboratory of Experimental Gastroenterology, [3] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Hepato-biliary-pancreatic surgery, [4] Institut Jules Bordet, Brussels, Belgium, Pathology, [5] Institut Jules Bordet, Brussels, Belgium, Laboratory of Molecular Immunology, [6] ULB, Brussels, Belgium, Faculty of Medicine, [7] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Pathology, [8] Institut Jules Bordet, Brussels, Belgium, Radiation-Oncology, [9] ULB, Brussels, Belgium, Pathology, [10] Hopital de La Pitié Salpétrière, Paris, France, Gastroenterology, [11] INSERM, France, Hepato-gastroenterology, [12] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Digestive Oncology.

Introduction: Pancreatic ductal adenocarcinoma (PDAC) remains one of the deadliest tumors. Unlike other tumors, the progress in systemic therapies is very slow, mainly due to the peculiar and resistant tumor microenvironment (TME) of PDAC. The addition of ablative stereotactic body radiation therapy (SBRT) in a total neoadjuvant strategy is promising for the treatment of localized PDAC and is currently being explored in several clinical trials including ours. However, if radiation therapy is known to possess the ability to modulate the TME, the molecular and immune effects of ablative SBRT are still poorly explored in human PDAC.
Aim: Here, we aim to characterize by RNA sequencing (RNAseq) and immunohistochemistry (IHC) analysis the immuno-molecular modulations in PDAC following isotoxic high-dose stereotactic body radiotherapy (iHD-SBRT).
Methods: Paraffin-embedded residual tumoral tissues of 50 localized PDAC resected between 2011 and 2020 were used: seventeen patients had surgery first, seventeen received an induction chemotherapy with FOLFIRINOX (FFX) only and sixteen with FFX followed by an iHD-SBRT designed to individually maximize the dose prescribed to the tumor and vessels interfaces up to Dmax(0.5cc)<53Gy in 5 fractions. After verification by an experienced pathologist, a quantitative analysis of the different IHC labelings was carried out using the Visiopharm™ software on the tumor area. RNA from the tumoral area was extracted using ALLPrep FFPE tissue kit (Qiagen®) and NGS libraries prepared using the QuantSeq Library Prep Kit for Illumina (Lexogen®). Differential gene expression (DGE) analyses were performed using Limma and edgeR packages from Bioconductor.
Results: Gene set enrichment analysis (GSEA) of RNAseq data demonstrate that iHD-SBRT is associated with a significant enrichment in classical cells and in basaloid cells (a subtype of basal cells associated with immunomodulatory stroma and better clinical outcomes) while being negatively associated with activated and inflammatory stroma. The gene ontology (GO) analysis shows multiple terms significantly enriched after iHD-SBRT related to the mitochondrial system, ribosomes and glutathione pathway suggesting these as potential candidates of interest for combination therapy with iHD-SBRT. Furthermore, our IHC data demonstrate that although collagen deposition increases significantly after iHD-SBRT (COL1: 83.27 vs 78.60 vs 68.04%, $p<0.001$ for iHD-SBRT, FFX and non-treated cohort respectively), the intra-tumoral lymphocyte infiltration is globally not altered, including for cytotoxic CD8+ lymphocytes. Only the CD4+ T helper population was significantly decreased after iHD-SBRT. While the FOXP3+ subpopulation was slightly increased after both types of induction therapy (FFX +/- iHD-SBRT), interestingly the xCell deconvolution algorithm showed that it was the CD4+Th2 cells that were decreased after iHD-SBRT. Regarding the macrophages population, no difference was observed for CD68+ cells expression. In parallel, xCell deconvolution analysis reveal that the M1 contingent is preserved after iHD-SBRTwhile the M2 macrophages are increased. Finally, after iHD-SBRT, the IHC expression levels of PD-L1 are significantly increased while PD-1 expression is significantly decreased.
Conclusions: iHD-SBRT seems associated with more classical and basaloid molecular subtypes related to better clinical prognosis and is able to durably immuno-modulate the TME of PDAC. Despite an increase in collagen deposit, the global lymphocyte infiltration is preserved after iHD-SBRT. We also identified several increased pro-tumoral cells and pathways after iHD-SBRT that could improve the development of better-oriented combination trials involving high-dose SBRT.

- O07 -

A RETROSPECTIVE OUTCOME ANALYSIS OF KRAS WILD TYPE AND KRAS MUTATED PANCREATIC ADENOCARCINOMA INCLUDING TARGETED DRUG THERAPIES. L. Mertens (1), F. Peeters (2), J. Jaekers (3), H. Topal (3), B. Topal (3), I. Vanden Bempt (4), G. De Hertogh (5), T. Roskams (5), X. Sagaert (5), C. Verslype (6), G. Rasschaert (6), F. Van Herpe (6), J. Dekervel (6) / [1] KUL - University of Leuven, Leuven, Belgium, Faculteit Geneeskunde, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Internal Medicine, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Abdominal Surgery, [4] University Hospitals Leuven (UZLeuven),

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Introduction: Pancreatic cancer is a devastating disease with poor prognosis, without significant improvement in outcome over the past 15 years. Ductal adenocarcinoma of the pancreas (PDAC) is the most common histological type, with a mutation in the KRAS oncoprotein in 85-90% of patients (RASmt). In the remaining 10-15% of PDAC patients a KRAS mutation is absent (RASwt) which opens doors to possible targeted therapies.
Aim: The aim of this study is to investigate KRAS-status and the prevalence of specific KRAS-mutations in a UZ Leuven pancreatic cancer cohort. Baseline characteristics and differences in disease free survival (DFS) and overall survival (OS) between different subgroups will be compared.
Methods: This retrospective, single-center study evaluated all patients covered by the pancreatic adenocarcinoma care program between January 2019 and February 2023 for inclusion with available molecular testing. Patients were subdivided between RASmt and RASwt patients. Neuro-endocrine tumors were excluded. Demographic, histopathological and molecular characteristics at baseline were extracted from the patients records. Data pertaining to the initial surgical or systemic therapeutic intervention, as well as subsequent treatment regimens upon disease progression, were gathered throughout a follow-up period extending until June 30th, 2023. A Fisher's exact test compared categorical variables between subgroups and Kaplan-Meier curves were constructed for OS and DFS of different subpopulations.
Results: A total of 233 patients diagnosed with pancreatic cancer were included in this study. This cohort consisted of 123 men (52,8%) and 110 (47,2%) women with a median age of 65 years (range 33-88 years). The majority of tumors were histopathologically classified as PDAC (86,3%), while mixed carcinoma accounted for 8%. Additionally, signet cell carcinoma, adenosquamous carcinoma, anaplastic carcinoma and acinar cell carcinoma were accounted for less than 1%. Upfront surgery was performed in 82 patients (35.2%), compared to 109 patients (46,8%) receiving palliative chemotherapy as first line treatment. Neo-adjuvant chemotherapy was administered to 42 patients (18,0%) with tumors categorized as borderline resectable. Of this group, 17 patients (7,3% of total cohort) remained unresectable while 25 patients (10,7% of total cohort) proceeded to surgery. In the whole cohort 213 tumors (91,4%) were RAS mutated (RASmt), consisting of 83 (39%) G12D, 73 (34%) G12V, 36 (17%) G12R, 3 (1.4%) G12C, 1 (0.5%) G12L, 1 (0.5%) G12A, 10 (4.7%) Q61H, 3 (1.4%) Q61L, 1 (0.5%) Q61K, 1 (0.5%) Q61R and 1 A146T (0.5%) mutations. Of the 20 patients with a RASwt tumor, 9 had a potentially targetable alteration. RASmt was found in 98 patients (91.6%) receiving surgery, and in 115 patients (91.3%) who had an unresectable tumor. First, a Fisher's exact test showed no significant difference in the prevalence of a KRAS mutation between patients undergoing primary surgery and patients receiving systemic therapy ($p = 0.98$). There was also no significant difference in the prevalence of KRAS G12D ($p = 0.6695$), KRAS G12V ($p = 0.3045$) and KRAS G12R ($p = 0.2525$) between both groups. Second, a Kaplan-Meier analysis in patients undergoing primary surgery, showed no significant difference in DFS between patients with a RASwt or RASmt tumor and between patients with a mutation in KRAS G12D, KRAS G12V or any other mutation in KRAS ($p=0.63$). Third, no significant difference in OS was observed between tumors with RASwt, a mutation in exon 2 (G12A, G12C, G12D, G12L, G12R and G12V) or a mutation in exon 3/4 (Q61H, Q61K, Q61L, Q61R and A146T) ($p=0.46$). Finally, OS showed no significant difference between patients with a mutation in KRAS G12D, KRAS G12V, KRAS G12R, other KRAS mutation or RASwt ($p=0.88$).
Conclusions: We report a unicentric, retrospective analysis of the molecular characteristics in patients with pancreatic cancer. Over 90% of tumors exhibited a RASmt, and no difference was observed for both DFS and OS with respect to different KRAS mutations nor when compared to patients with a RASwt tumors. It is important to remark that the sample size of the RASwt group was very limited. However a potential targetable oncogenic driver mutation was found in almost half of the RASwt patients.

- O08 -

THE RADIOLOGICAL MORPHOLOGY OF MESOPANCREAS, A NEW VARIABLE TO PREDICT A POSITIVE VASCULAR MARGIN AFTER PANCREATODUODENECTOMY FOR PANCREATIC DUCTAL ADENOCARCINOMA?

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Introduction: While the main goal of surgery for curative treatment of pancreatic ductal adenocarcinoma (PDAC) is to perform a R0 resection, the most frequently invaded surgical margins on pancreaticoduodenectomy (PD) specimens are vascular margins at the level of the superior mesenteric vein and especially the superior mesenteric artery (SMA), the latter also being called mesopancreatic margin. The mesopancreas consists of the adipose tissue between uncinate process and SMA, containing blood and lymphatic vessels, lymph nodes and nerve fibers. Considering embryology, it

may be hypothesized that PDAC tumor cells tend to infiltrate the retroperitoneum through the contents of mesopancreas, justifying the frequent positive margin at this level.
Aim: Because the radiological aspect of mesopancreas has been poorly studied, the aim of the study was to assess the mesopancreatic infiltration on diagnostic imaging, corroborate with the corresponding margin histopathology and evaluate the impact on survival in PDAC patients who underwent PD.
Methods: From 2015 to 2021, all patients who underwent PD for PDAC with curative intent were reviewed from a prospective database, excluding patients lost to follow-up, who died postoperatively or within the first year for non-oncological reason, and those with unavailable preoperative imaging. The surgical margins of pathological specimens were reviewed; margin involvement (R1) was defined in case of tumoral cells ≤1mm. Blinded reviewing of radiographic images was conducted on contrasted-enhanced computed tomography (or magnetic resonance imaging if unavailable). According to qualitative assessment, the mesopancreas tissue was defined as normal fat, fat stranding or solid infiltration.
Results: In total, 133 patients were included in the study, including 51 (38%) who received neoadjuvant therapy. The location of the tumor was into the head or the uncinate process in 54% and 46%, respectively. At diagnosis, PDAC were classified as resectable (51%), borderline resectable (28%) and locally advanced (9%) according to the NCCN classification. Fat stranding or solid tumoral infiltration in the mesopancreas was present in 45 (34%) and 18 (14%) patients, respectively. Tumor location, chronic obstructive pancreatitis, vascular contacts and NCCN resectability were associated with mesopancreas infiltration at univariate analysis ($p<0.001$). Median overall and disease-free survivals were significantly lower in case of solid infiltration compared to normal fat and fat stranding in the mesopancreas. When comparing the patients with mesopancreatic fat stranding at diagnosis who received neoadjuvant therapy (n=20) to those who underwent upfront surgery (n=25), no significant impact was observed in disease-free and overall survivals. R0 resection was obtained in 36%; in all patients with R1 resection, a vascular margin was involved. Tumor size, SMA margin and resection status were associated with mesopancreas infiltration on diagnostic imaging. Prognostic factors associated with OS and DFS at univariate analysis were tumor location, SMA radiological contact, mesopancreas radiological infiltration, tumor size, lymph nodes status, perineural and microvascular invasion, and SMA margin.
Conclusions: The solid infiltration of mesopancreas on diagnostic imaging was associated with a poor prognosis, but not fat stranding, in patients who underwent PD for PDAC. SMA margin and resection status were correlated with the radiological texture of the mesopancreas. Tumors located in the uncinate process have a poorer survival compared to cephalic tumors, which could question on the implication of the mesopancreas in the retroperitoneal tumor growth.

- O09 -

CORRELATION OF THE VOLUME OF THE LIVER GRAFT MEASURED WITH CT & MRI, COMPARED WITH THE INTRAOPERATIVE DATA. E. Danse (1), D. Lacomblez (2), L. Coubeau (3), O. Ciccarelli (3), E. Bonaccorsi-Riani (3), C. de Magnee (3), R. Reding (3), N. Michoux (2) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Radiology, [2] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Imaging, [3] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Transplantation and abdominal Surgery.

Introduction: In the most recent surgical treatments for colorectal cancer liver metastases, liver transplantation is playing a crucial place. Imaging plays a key role in estimating the volume of liver tissue transplanted. A limited number of studies have focused on the analysis of the accuracy of hepatic volumes estimated on the basis of CT and/or MRI. in relation to the in vivo liver volume.
Aim: To evaluate the agreement between the liver graft weight from living donors measured with CT and MR and the intraoperative weight, and to reassess the common conversion formula .
Methods: In 32 consecutive adults liver donors preoperatively evaluated with CT and MR, we compared retrospectively CT- and MRI-based volumetries of the resected liver segments done by 2 radiologists with dedicated software (Intellispace Portal for CT, Vitrea Software for MRI) to intraoperative weight (IW). Imaging volumes were converted into weight using a surgical formula (F1= volume*0.9) and an imaging formula (F2=206.3+0.653*volume). Inter-reader and inter-technique reproducibility of volumetry were studied using Bland-Altman methodology. Linear regression model based on the mean volumetry from both readers was performed to reconstruct a conversion formula (F3) to be compared to (F1)/(F2).
Results: Inter-reader agreement on volumetry was achieved with a precision of ±44ml regardless of the imaging technique. Inter-technique agreement was achieved with a precision of ±88ml. Agreement between (F1)MRI / (F1)CT and IW was achieved with a precision of ±75g [56g;94g] / ±86g [65g;108g]. Agreement between (F2)MRI / (F2)CT and IW was achieved with a precision of ± 85g [63g;106g] / ±92g [69g;115g], with a significant bias (overestimation from imaging techniques) of -43g [-74g;-13g] / -57g [-90g;-24g] respectively. Regression analysis yielded (F3)MRI: weight=55.2+0.81*volume and (F3)CT: weight=46.7+0.80*volume, achieving a precision of ±71g [53g;89g] / ±81g [61g;102g] with IW.
Conclusions: Inter-reader agreement on volumetry is independent of the imaging technique. A slightly better agreement with IW is obtained with MRI. Conversion formulas with a slope coefficient close to 0.8-0.9 yield a weight value in better agreement with IW.

- O10 -

PROGNOSTIC VALUE OF CIRCULATING CYTOKINES IN CHEMOREFRACTORY COLORECTAL CANCER. I. Assaf (1), D. Fimereli (2), G. Anthoine (3), R. Fazio (4), V. Dapra (4), A. Audisio (4), T. Akin Telli (4), M. Van Hooren (4), R. Saude Conde (4), G. Bregni (4), A. Hendlisz (1), F. Sclafani (1) / [1] Institut Jules Bordet, Brussels, Belgium, Department of Digestive Oncology, Institut Jules Bordet, The Brussels University Hospital, Brussels, Belgium, [2] Institut Jules Bordet, Brussels, Belgium, Breast Cancer Translational Laboratory, Bordet Cancer Research Laboratory, [3] Institut Jules Bordet, Brussels, Belgium, GI Cancer Laboratory, Bordet Cancer Research Laboratory, Institut Jules Bordet, [4] Institut Jules Bordet, Brussels, Belgium, Department of Digestive Oncology, Institut Jules Bordet.

Introduction: The prognosis of chemorefractory metastatic colorectal cancer patients remains poor despite the increased number of active treatments. Liquid biopsy is a revolutionary tool in the oncology field. However, the bulk of research has so far focused on circulating tumor DNA. While involved in a plethora of physiological processes, cytokines play an important role in cancer formation, development and progression, and could be optimal biomarkers for prognostication and management decisions in colorectal cancer. Very little, however, is known about the potential role and clinical applications of circulating cytokines in chemorefractory colorectal cancer.
Aim: The objective of the study was to assess the prognostic value of a large panel of circulating cytokines in a well clinically-annotated population of patients with chemorefractory colorectal cancer.
Methods: This was a retrospective, single-center study conducted at the Institut Jules Bordet. Chemorefractory colorectal cancer patients were eligible if they had a blood sample prospectively taken at baseline (i.e., before the start of a new line of systemic treatment) within the context of an academic clinical trial. The study population consisted of a discovery and a validation cohort. In the discovery cohort, 182 circulating cytokines were retrospectively tested with a commercially available, semi-quantitative multiplex assay (Human L182 Array, Membrane, RayBio). Prognostic cytokines were analyzed in the validation cohort by an enzyme-linked immunosorbent (ELISA). Eight healthy volunteers were included in the study, and donated blood samples to set the cut-off for each of the cytokines tested in the validation cohort. Overall survival (OS) was the primary outcome measure, and measured from the collection of the baseline blood sample to death from any cause. Standard bioinformatics and statistics were used, including the false discovery rate (FDR) method with a significance level of <0.01 to correct for multiple comparisons.
Results: Eighty-five patients were included in the discovery cohort. Of the 182 cytokines analyzed, only 4 were found to be associated with OS, meeting the criteria for statistical significance at the FDR threshold of <0.01: insulin-like growth factor-binding protein 1 (IGFBP-1) (HR 2.1 [95%CI:1.58-2.79], FDR<0.001), insulin-like growth factor-binding protein 2 (IGFBP-2) (HR 1.65 [95%CI:1.28-2.13], FDR=0.006), serum amyloid A (SAA) (HR 1.84 [95%CI:1.39-2.43], FDR<0.001), and Angiotensin II (HR 1.65 [95%CI:1.29-2.1], FDR=0.006). The validation cohort consisted of 111 patients. In univariable analysis, IGFBP-1 (HR 2.04 [95%CI: 1.20-3.45], FDR=0.024), IGFBP-2 (HR 4.17 [95%CI: 2.08-8.33], FDR=0.001), and serum amyloid A (SAA) (HR 2.13 [95%CI: 1.43-3.23], FDR=0.001), were significant prognostic factors. After adjusting for baseline prognostic factors, the association with OS was confirmed for IGFBP-1 (HR 2.70 [95%CI: 1.56-4.76], FDR=0.006) and IGFBP-2 (HR 3.33 [95%CI: 1.61-6.67], FDR=0.008), while only a trend was observed for SAA (HR 1.54 [95%CI: 0.99-2.44], FDR=0.092). High concentrations of IGFBP-1 and/or IGFBP-2 were detected in 24 (21.6%) patients. These had a worse OS than those with low concentrations of both IGFBP-1 and IGFBP-2 (3.0 vs 6.9 months, HR 2.44 [95%CI: 1.52-4.0], FDR=0.002). In a multivariable analysis, the independent prognostic role of the combined assessment of IGFBP-1 and IGFBP-2 was confirmed (HR 3.03 [95%CI: 1.79-5.0], FDR<0.001).
Conclusions: In this study, we analyzed the largest ever-analyzed panel of circulating cytokines in a population of chemorefractory colorectal cancer. According to our findings, circulating IGFBP-1 and IGFBP-2 are independent prognostic biomarkers, high levels of these being associated with worse survival. These results are consistent with the extensive literature supporting an association between the IGF pathway and colorectal cancer. Further research, however, is needed to confirm our findings in larger independent series, and to elucidate the biological mechanisms underlying the putative prognostic effect of these cytokines.

- O11 -

CLINICAL OUTCOMES AFTER SURGERY FOR PROGRESSIVE LESIONS IN OLIGOPROGRESSIVE METASTATIC MMR-DEFICIENT GASTRO-INTESTINAL CANCER: A CASE SERIES. P. Perremans (1), F. Van Herpe (2), G. Rasschaert (2), J. Van Ongeval (3), J. Decaestecker (4), B. Topal (5), H. Topal (5), G. Bislenghi (5), A. Wolthuis (5), E. Van Cutsem (2), J. Dekervel (6) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Digestive Oncology, [3] AZ Sint-Lucas, Ghent, Belgium, Gastroenterology and Digestive Oncology, [4] AZ Delta, Roeselare, Belgium, Gastroenterology, Digestive Oncology and Hepatology, [5] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Abdominal Surgery, [6] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Digestive Oncology.

Introduction: Immune checkpoint inhibitors have demonstrated improved clinical outcomes in the majority of patients with MMR-deficient gastrointestinal cancers. In the setting of oligoprogression, recent evidence suggests that local therapy or resection could be a viable alternative to the existing standard of care.
Aim: Through this case series, we try to assess the feasibility and safety of local surgical resection in the management of oligoprogressive disease.
Methods: Patients with oligoprogressive metastatic MMR deficient gastro-intestinal cancer treated with ICI (im-mune checkpoint inhibition) and local resection between 2014 and 2023 were included from 3 centres in Belgium. Follow-up and survival are reported from surgery onwards.
Results: We included 9 patients, predominantly with MMR deficient colorectal cancer. All patients received local resection of a progressive lesion. All surgeries were performed successfully with R0 resection in 8 out of 9 cases. Only one patient experienced post operative complications. The PFS at time of inclusion was 88% with a median follow up time of 12 months.
Conclusions: Resection of progressive lesions in selected patients with oligoprogressive stage IV MMR-deficient gastro-intestinal cancer is feasible and safe and should be considered as a viable treatment strategy. Further prospective research is imperative to confirm these findings and change current treatment guidelines.

- O12 -

SELECTIVE INTERNAL RADIATION THERAPY FOR NEUROENDOCRINE LIVER METASTASES: EFFICACY, SAFETY AND PROGNOSTIC FACTORS. A RETROSPECTIVE SINGLE INSTITUTION STUDY. D. Briol (1), A. Ceratti (1), L. Annet (2), C. Dragean (2), E. Danse (2), P. Trefois (2), R. Lhommel (3), P. Goffette (2), M. Van Den Eynde (1), A. De Cuyper (1), I. Borbath (4) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Oncology, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Radiology, [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Nuclear Medicine, [4] Cliniques universitaires Saint-Luc, Brussels, Belgium, Gastroenterology.

Introduction: Selective internal radiation therapy (SIRT) has shown promising results in unresectable liver metastases from neuroendocrine neoplasm (NENLMs) with a high disease control rate (DCR) of 91% reported in a multicenter study (Braat A.J. et al., 2019).
Aim: We designed a retrospective study to assess the efficacy and safety of 10y of SIRT in this indication, and looked for prognostic factors of efficacy.
Methods: This study included 50 consecutive patients suffering from NENLMs who underwent SIRT from 2011 to 2021, in our center. Median age was 63.4 years, sex ratio (male/female) was 1.17. The two major NEN primary anatomical sites were pancreas (46%) and small intestine (36%). Histological NEN grades were 10%, 46% and 44% for grades 1, 2 and 3 respectively. Primary endpoint was tumour objective response (OR=CR+PR) and disease control rate (OR+SD=DCR) according to RECIST 1.1, at 2, 4 and 12 months after SIRT. Secondary endpoints were overall survival (OS), liver progression-free survival (liver-PFS), clinical response (NEN related symptoms improvement) and safety.
Results: OR and DCR were 16% and 80% at 2 months, 22% and 92% at 4 months and 32% and 82% at 12 months. Median OS from SIRT was 94,2 months and survival rates at 1 and 2 years were 76% and 72% respectively. Median liver-PFS was 13,6 months. Significant prognostic factors for OS and liver-PFS were 1. NEN histological grade (3 versus 1+2) (hazard ratio (HR) for OS: 4.33 [1.77-10.57], for liver-PFS: 3.91 [1.34-11.37]) and 2. Early DCR (HR for OS: 0.14 [0.05-0.37], for liver-PFS: 0.016 [0.003-0.078]). Improvement of pretreatment NEN related symptoms occurred in 7 of the 10 symptomatic patients (5 patients had flushing, 3 patients diarrhea, 1 patient concomitant flushing and diarrhea and 1 patient hypoglycemia). Grades 3–4 adverse events were lymphocytopenia (12%) and anicteric cholestasis (6%). One patient died from radioembolization-induced liver disease (REILD) 7 months after administration of SIRT, already suspected on the Yttrium-90-Time-of-flight PET-CT performed at day+1 post-treatement. This patient had a suspected underlying liver disease, possibly related to chronic alcohol consumption.
Conclusions: In our experience, SIRT showed efficacy in NENLMs patients, with a high DCR and with an acceptable safety profile. Low NEN histological grade and early DCR were associated with a better OS and liver-PFS.

- O13 -

NEOADJUVANT IMMUNE CHECKPOINT INHIBITION IN LOCALLY ADVANCED MMR-DEFICIENT COLON CANCER: A CASE EXPOSING CURRENT UNMET NEEDS. J. Van Durme (1), A. Jans (1), Z. Hu (1), A. Peddle (1), A. Billiet (2), F. Van Herpe (2), X. Sagaert (3), A. Wolthuis (4), S. Tejpar (5), G. Rasschaert (5) / [1] KUL - University of Leuven, Leuven, Belgium, Laboratory of Digestive Oncology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Pathology, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Abdominal Surgery, [5] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology & Laboratory of Digestive Oncology.

Case Report: Over the past few years, a rise in neoadjuvant trials is observed in clinical GI-oncology research. The most striking results to date come from the use of neoadjuvant immune checkpoint inhibition (ICI) in locally advanced DNA

mismatch repair deficient (dMMR) colon cancer (CC). In NICHE-2, non-metastatic dMMR CC was treated with one dose of ipilimumab (1mg/kg) and two doses of nivolumab (3mg/kg), followed by surgery in ≤6 weeks of registration. Major pathological response was seen in 95%, while 67% had complete response (pCR). Although definitive results are yet to be published, two principal questions arise. Is it already prime time for upfront and neoadjuvant use of ICI in dMMR CC? And can we ultimately evolve towards an organ sparing strategy?
We present a case of a 52-year-old male with abdominal pain who was diagnosed with a subobstructive adenocarcinoma in the colon descendens, dMMR, microsatellite instability high (MSI-H), clinically staged cT4N3M0. Germline screening showed a pathological mutation in the MSH2 gene. After thorough discussion with the patient and at the multidisciplinary tumor board it was decided to start off-label neoadjuvant ICI. After 3 cycles of pembrolizumab 200mg, cross sectional imaging suggested some response (cT3N2M0), while colonoscopy still showed a bulky stenosing tumor with negative biopsies. Three weeks later a laparoscopic left hemicolectomy was performed. Pathology returned as a pT0N0 specimen with 27 out of 27 lymph nodes negative. Acellular mucus lakes were observed transmurally without viable tumor cells. More curious however, was the observation of a tubular adenoma with high grade dysplasia in direct proximity, thus appearing untouched by systemic treatment with ICI. Pembrolizumab was continued for a total of six months. Clinical follow up runs flawless.
The observations in this remarkable case demonstrate that the upfront use of ICI in dMMR CC is an attractive strategy. The untouched precursor lesion suggests subsequent organ sparing strategies should today only be pursued with greatest of caution and consent. However we do believe surgery is overtreatment in selected cases. Therefore there is a clear need to understand the type and depth of response to ICI. Today we lack reliable predictors for complete pathology response and above all there is still a huge gap between clinical and pathology staging. While dMMR/MSI-H serves as a predictor to ICI, it is insufficient to address all our questions. This might potentially be driven by intralesional MSI heterogeneity. Since the detailed results of the NICHE-2 study are yet to be published, potentially the most interesting mechanistic data might come from the non- or partial responders. The advent of cutting edge techniques like single-cell and spatial transcriptomics might help resolve these questions. Although we do believe this one single case might not address all these questions. A planned deep dive into this tissue, and that of other MSI-H non responders from our clinic, exploring the immune and epithelial phenotypes, might guide the quest towards a thorough classification of predictive subtyping for the use of neoadjuvant ICI. Next to that, ongoing trials with next generation ICI both in the context of dMMR and pMMR CC will also address these unmet needs.

- O14 -

CONTINUING SOMATOSTATIN ANALOGUES UPON PROGRESSION IN NEUROENDOCRINE TUMOR PATIENTS (SAUNA TRIAL) — STUDY PROTOCOL FOR A BI-NATIONAL, MULTI-CENTER, OPEN-LABEL, RANDOMIZED, PRAGMATIC CLINICAL TRIAL. S. Chhajlani (1), J. Kuiper (2), I. Borbath (3), W. Dercksen (4), C. Deroose (5), S. Heemskerk (6), S. Polinder (6), E. Roelant (7), I. Verhaegen (7), I. Van der Massen (1), A. Walenkamp (8), W. de Herder (2), M. Peeters (1), J. Hofland (2), T. Vandamme (1), SAUNA investigators (9), Dutch Belgian Neuroendocrine Tumor Society (10) / [1] UZA (Universitair Ziekenhuis Antwerpen) - NETwerk, Edegem, Belgium, Medical Oncology, [2] Erasmus MC, University Medical Center Rotterdam, The Netherlands, Internal Medicine, [3] UCL Saint-Luc, Brussels, Belgium, Digestive Oncology, [4] Máxima MC, Eindhoven, The Netherlands, Internal Medicine, [5] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Nuclear Medicine, [6] Erasmus MC, University Medical Center Rotterdam, The Netherlands, Public Health, [7] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Clinical Trial Center, [8] University Medical Center Groningen, Groningen, The Netherlands, Medical Oncology, [9] UZA (Universitair Ziekenhuis Antwerpen) - NETwerk, Edegem, Belgium, NA, [10] DBENTS, Belgium, The Netherlands, NA.

Introduction: Gastroenteropancreatic neuroendocrine tumors (GEP NET) are malignant neoplasms that impact survival and quality of life (QoL). Somatostatin analogs (SSA) are used for treating hormonal symptoms caused by GEP NET and have antiproliferative effects. They are used as first-line therapy in advanced GEP NET patients, but disease control is limited to a median of 14–32 months. Second-line treatment options include targeted therapy (everolimus or sunitinib), or peptide receptor radionuclide therapy (PRRT) with 177Lu-DOTATATE. In patients suffering from a NET-related hormonal syndrome, SSA is generally continued life-long. However, there is no consensus on whether it is beneficial to continue SSA in non-functional NET upon disease progression. Moreover, the current European Neuroendocrine Tumor Society (ENETS), European Society of Medical Oncology (ESMO), and the North American Neuroendocrine Tumor Society (NANETS) guidelines provide insufficient support in this area. Consequently, routine clinical practice differs between NET centers in both Belgium and the Netherlands. Feasibility questionnaires in SAUNA participating centers revealed a lot of inter- and intra-country variability in current clinical practice regarding SSA use in this setting. During second-line therapy with everolimus, 58% of all centers (n=19) would continue SSA (67% of the Belgian centers (n=13) and 16% of the Dutch centers (n=6)). A similar trend was seen for sunitinib as a second-line treatment. For patients treated with PRRT, 47% of all centers (n=19) would continue SSA (46% of the Belgian centers (n=13) and 50% of the Dutch centers (n=6)). Due to the ongoing activity of the somatostatin receptor pathway in GEP NET progressing on first-line SSA, we hypothesize that SSA have an added efficacy in second-line therapy.

Aim: To study the efficacy of SSA continuation during second-line therapy in advanced GEP NET.
Methods: The SAUNA trial (clinicaltrials.gov.: NCT05701241) is a bi-national, multi-center, open-label, randomized, pragmatic clinical trial. It will be conducted across 19 participating centers in Belgium and the Netherlands. A total of 270 patients with advanced, non-functional grade 1 or 2 GEP NET and progression under first-line SSA will be included in the trial. Per the investigator's choice of second-line therapy, patients will be included in into study arm 1 (n=142) or study arm 2 (n=128). Study arm 1 will include patients receiving PRRT with four cycles of 177Lu-DOTATATE, and study arm 2 will include patients receiving targeted therapy (everolimus or sunitinib). Thereafter, they will be randomized (1:1) per study arm between SSA continuation or withdrawal. Follow-up will be performed every three months until 18 months after start of second-line therapy. After the treatment phase, participants will be followed up for five years (long-term follow-up). Follow-up will consist of imaging and Response Evaluation Criteria In Solid Tumors (RECIST) 1.1 assessment, validated questionnaires and optional blood collection for biomarker analysis.
Results: Co-primary endpoints are improvement in progression-free survival (PFS) according to the RECIST 1.1 criteria and in time to deterioration (TTD) of quality of life (QoL) per EORTC-QLQC30 questionnaire per study arm with a HR of 0.54 and 0.55, respectively. Secondary endpoints include PFS at 18 months, difference in pooled PFS and TTD of both study arms, overall survival, response rates, QoL, medical costs, cost-effectiveness, and toxicity. Exploratory endpoints include biomarker analyses (e.g., circulating tumor DNA [ctDNA], circulating transcripts, circulating non-malignant DNA, etc.) in a subset of participants to discover additional blood-based biomarkers for prediction of response to therapy to better select patients that will benefit from SSA therapy. We additionally aim to perform a dedicated cost-effectiveness analysis, so healthcare systems can be informed about the health economic consequences of this strategy. The study received ethical committee approval on 31/05/2023. Currently, patient recruitment is ongoing.
Conclusions: The trial is poised to provide necessary high-grade evidence for guidelines and inform the NET specialists on the preferred strategy regarding the efficacy of SSA continuation during second-line therapy in terms of PFS, QoL and cost-effectiveness. This is an independent trial funded by The Belgian Health Care Knowledge Centre and ZonMw, Belgium - Netherlands Funding of International Trials (BeNeFIT; 21577).

- O15 -

APPORT DE L'ENDOSCOPIE DANS LE DIAGNOSTIC DES CANCERS GASTRIQUES EN RÉPUBLIQUE DÉMOCRATIQUE DU CONGO. A PROPOS DE 3068 ENDOSCOPIES DIGESTIVES HAUTES À L'HÔPITAL GÉNÉRAL DE RÉFÉRENCE DE PANZI/BUKAVU. M. Josue (1), C. Chassinga Baharanyi (2), C. Mugisho Mastaki (1), G. Byabene (3), M. Van Gossum (4) / [1] Panzi Hospital DR Congo, Bukavu, Democratic Republic of Congo, gastroenterology, [2] Panzi Hospital DR Congo, Bukavu, Democratic Republic of Congo, anatomopathology, [3] Panzi Hospital DR Congo, Bukavu, Democratic Republic of Congo, surgery, [4] CHU Saint-Pierre, Brussels, Belgium, Gastroenterology.

Introduction: Le cancer de l'estomac est un problème majeur de santé publique, la disponibilité des moyens diagnostiques peut améliorer la prise en charge en Afrique.
Objectif: Etudier l'intérêt de l'endoscopie dans la prise en charge des cancers de l'estomac dans le département de la médecine interne de l'Hôpital Général de Référence de Panzi/ Bukavu.
Méthodes: Il s'agissait d'une étude transversale descriptive et analytique réalisée dans les services de Gastro-entérologie et d'anatomopathologie de l'Hôpital Général de Référence de Panzi, portant sur 3068 patients dont 161 cas de cancer confirmés à l'anapathomo patologie, sur une période de 9ans. Les cas ont été colligés à partir des registres et des dossiers des patients. Nous avons analysé les caractéristiques épidémiologiques notamment l'âge, le sexe, la provenance; les caractéristiques clinico-biologiques, endoscopiques, anatomopathologique et thérapeutique par le logiciel SPSS 23. L'interprétation des résultats sous forme de pourcentages et P-value, avec une significativité statistique si $p < 0,05$.
Résultas: La prévalence des lésions cancéreuses de l'estomac est de 5,24%, dont 57% des hommes et 43% des femmes. L'âge moyen étant de 56,23±13,04ans. Les facteurs associés à cette maladie sont : Cliniquement l'épigastralgie dans 93,17%, la Tradithérapie 52,80% avec p=0,01204, l'antécédent d'ulcère gastrique dans 45,30% avec p=0,0000 , suivi pour Helicobacter pylori dans 33,50% avec p=0,0000 et Tabac 24,20% avec p=0,0236. La sensibilité épigastrique dans 94,40% et la pâleur cutanéomuqueuse dans 45,58%. La forme ulcéro-bourgeonnante chez 40.37% des malades. L'adénocarcinome qui était le type histologique le plus représenté avec 96.9%. Dans notre étude 83,22% des cancers étaient associés à l' H. Pylori à l'anapath. 50.31% de nos patients avaient les métastases ganglionnaires et hépatiques ou pulmonaires. Le refus de traitement est de 50.31% de nos patients. Chez ceux qui ont adhéré : 31,05% avaient bénéficié de la chirurgie curative et 11,20% ont bénéficié la chirurgie palliative. Dans l'évolution : 52.17% de perte de vue et 31.06% des patients qui étaient décédés dans les 6mois. L'adénocarcinome est significativement lie à la mauvaise avec un p=0,0000
Conclusions: Le cancer de l'estomac est un problème de santé publique en Afrique; plus les malades ont accès à l'endoscopie plus la prévalence augmente. Notons qu'un diagnostic précoce, l'éradication de l'HP, ainsi que la prévention d'autres facteurs de risque permettront une prévention contre les cancers de l'estomac. Mots-clés : épidémiologie, clinique, anatomopathologique, adénocarcinome, Helicobacter pylori, estomac.

- O16 -

A NOVEL DELETION MUTATION IN GAPPS: INSIGHTS FROM A COMPREHENSIVE FAMILY-BASED CASE ANALYSIS. C. Van Laeken (1), J. Callens (2), A. Van Goethem (3) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Gastroenterology , [2] AZ Klina, Brasschaat, Belgium, Department of Gastroenterology, [3] AZ Klina, Brasschaat, Belgium, Department of Oncology.

Introduction: Gastric adenocarcinoma and proximal polyposis of the stomach (GAPPS) is a rare familial syndrome with an autosomal dominant inheritance pattern. It is characterized by fundic gland polyposis of the gastric body and is associated with a significant risk of gastric adenocarcinoma.
Aim: The purpose of this family-based case analysis was the clinical and pathological characterisation of a new mutation found within GAPPS.
Methods: The members of the investigated family underwent gastroscopy and genetic analysis by bi-directional Sanger sequencing of the adenomatous polyposis coli (APC) promoter IB. A novel deletion of nucleotide -191 C was revealed as the underlying genetic mutation associated with GAPPS.
Results: A 56-year-old woman who presented with epigastralgia underwent gastroscopy, which revealed over 100 glandular polyps in the corpus and fundus. Further investigation using PET-CT raised concern for a possible malignant gastric tumor without significant glandular protrusions or metastases. In view of the clinical findings, a multidisciplinary decision was made to perform a prophylactic total gastrectomy, as GAPPS was suspected. Histologic examination of the gastrectomy confirmed FGP (fundic gland polyps) with no evidence of a cancerous lesion. Genetic analysis revealed a novel deletion of nucleotide -191 C in the APC promoter IB, which is associated with GAPPS. The patient's family history revealed an autosomal dominant inheritance pattern, as her mother and sister had died of gastric cancer and the patient's brother, daughter, son and niece were endoscopically diagnosed with fundic gland polyposis. Genetic analysis is now ongoing in all the family members. The genomic mutation has already been identified in the patient's brother, where a prophylactic laparoscopic total gastrectomy is planned.
Conclusions: This family-based case analysis significantly enhances our understanding of GAPPS by uncovering a previously unknown deletion mutation. The distinctive endoscopic course observed in this family, in combination with the identification of a novel mutation in the APC gene promoter IB, offers valuable insights for clinicians.

- O17 -

PROGNOSIS AFTER CURATIVE RESECTION OF NON-METASTATIC PANCREATIC NEUROENDOCRINE TUMORS: A RETROSPECTIVE TERTIARY CENTER STUDY. T. Hendrickx (1), J. Vancanneyt (1), J. Dekervel (1), G. Rasschaert (1), F. Van Herpe (1), J. Jaekers (2), H. Topal (2), B. Topal (2), C. Deroose (3), V. Vandecaveye (4), C. Verslype (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and hepatology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Abdominal surgery, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Nuclear Medicine, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Radiology.

Introduction: Neuroendocrine tumors (NETs) are a rare and heterogenous group of tumors that arise from neuroendocrine cells throughout the body and are able to produce peptides resulting in characteristic hormonal syndromes. There is a worldwide increasing incidence over the last decades, mostly due to the increased use of radiographic imaging. As a consequence, there is an increase in surgical resections for NETs with pancreatic NETs (pNETs) being the second most frequent cause of pancreatic surgical resection after pancreatic adenocarcinoma. Although radical surgery is regarded as the only curative treatment, the benefits of surgery must be outweighed against the perioperative morbidity and mortality. However, when curative resection is performed, it remains difficult to predict recurrence, resulting in debatable follow-up strategies for this heterogeneous group of tumors. The past decades, several studies have tried to provide an answer to this question by establishing prognostic scoring systems and normograms to predict recurrence. In our study we aim to determine long-term results, recurrence patterns as well as the clinical and pathological factors that impact recurrence and overall survival (OS) in well-differentiated non-metastatic pNETs treated with curative surgery.
Aim: The aim of our study was to determine long-term results, recurrence patterns as well as the clinical and pathological factors that impact time-to-recurrence (TTR), recurrence-free survival (RFS) and overall survival (OS) in well-differentiated non-metastatic pNETs treated with curative surgery.
Methods: Data of all patients who received radical surgery with curative intent for non-metastatic well-differentiated pNETs were obtained from a prospectively maintained database of the University Hospitals Leuven. Data from September 2002 until November 2021 were retrospectively analyzed. Patients with metastatic disease and/or neuro-endocrine carcinoma (NEC) were excluded. Median follow-up time was calculated using the Reverse Kaplan Meier method. A Cox proportional hazards model was used to assess variables associated with recurrence.
Results: The study included 128 patients. Only 8 patients (6.25 %) had recurrent disease with a median follow-up of 44.38 months (29.80-74.68). The median TTR was 38.70 months (18.04-46.16). Univariate analysis showed that Multiple Endocrine Neoplasia 1 (MEN-1) and R1-status are statistically significant predictors for disease recurrence.
Conclusions: In this series of 128 patients with non-metastatic well-differentiated pNETs only 6.25% had recurrent disease after curative resection. MEN-1 and R1-status were found as predictors for recurrence in univariate analysis.

BELGIAN PANCREATIC CLUB (BPC)

- P01 -

EVALUATION AND PREDICTIVE FACTORS OF LONG-TERM NUTRITIONAL SUPPORT IN MODERATE TO SEVERE ACUTE PANCREATITIS REQUIRING INTERVENTION: A RETROSPECTIVE STUDY. M. Fernandez (1), A. Hadefi (2), M. Arvanitakis (2) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology, [2] Erasme Hospital, Brussels, Belgium, Gastroenterology.

Introduction: Moderate to severe acute pancreatitis (AP) may occur in up to 20% of the AP cases and is associated with a significant rate of organ failure (OF), need for interventions, and death. The pro-inflammatory process, collections, and necrosis will increase the body's protein-energy needs. In most patients with moderate to severe AP, oral feeding will not be possible in the initial course of the disease and not enough after the resolution of AP. Therefore, nutritional support (NS) is one of the most essential cornerstones in managing moderate to severe AP. Numerous meta-analyses and randomized studies showed the superiority of enteral nutrition (EN) over parenteral nutrition (PN). EN maintains the integrity of the intestinal barrier, ensures intestinal motility, reduces the risk of bacterial translocation, and increases splanchnic blood flow, consequently decreasing complications. Nevertheless, PN will be necessary in patients with EN intolerance or sometimes in combination with EN if nutritional targets are unmet. NS's type, route, and duration have not been widely investigated in moderate to severe patients requiring multiple interventions and long-term hospital stays (> 30 days). Consequently, predictive factors for home NS after patient discharge are also lacking.
Aim: We aimed to evaluate long-term NS modalities and predictive factors for home NS in patients with moderate to severe acute pancreatitis requiring multiple interventions.
Methods: We performed a retrospective study of patients with moderate to severe AP with a hospital stay > 30 days requiring intervention for collections treated in our endoscopy unit between 1/1/2015 and 31/12/2022 and evaluated their NS. Exclusion criteria were the following: hospital stay < 30 days, no intervention, chronic pancreatitis, and pancreatic cancer. Baseline characteristics, laboratory results, interventions, and NS information were gathered by reviewing patient's records and our endoscopic database.
Results: One hundred thirty-six patients with moderate to severe AP requiring interventions were identified, and 48 patients met all the criteria. Baseline characteristics are the following: majority of men (77%), mean age of 51 years (SD 15), mean body mass index (BMI) of 28 (SD 6), and mean hospital stay of 91 days (SD 7). The main etiological factors were biliary stones (35%) and alcohol (31%). According to the Revised Atlanta Classification, moderate and severe were represented in 54 and 46 % of the cases, respectively. 85,4% (41/48) of the patients required intensive care unit (ICU) admission, 81,3% (39/48) presented organ failure (OF) and 67% (26/39) persistent OF. Mortality was observed in 23% of the cases (11/48). Regarding interventions, 91% (44/48) of patients required endoscopic drainage, and 60,4% (28/48) underwent direct endoscopic necrosectomy with a mean number of 2 procedures (0-7), 27% (13/48) percutaneous drainage, whereas surgical drainage was necessary for two patients. Regarding nutrition, the mean weight loss percentage between admission and the first 30 days of hospitalization was 15,6 kg (SD 8,7). Before 30 days of length stay, 44 patients (92%) required NS (50% EN, 13% PN, 29% combined EN and PN). Forty-seven patients (98%) required a prolonged NS (> 30 days), including 43 with EN and 31 with PN. Home NS was necessary for 11 patients (23%): EN in 9 patients (five percutaneous gastrostomy with jejunal prolongation and four direct jejunostomy) and PN in 2 patients. The median duration of NS was 71 days (14-254). 77% of patients had a final good clinical outcome. Due to a small number of patients (n=11), no significant predictive factor of home NS was identified.
Conclusions: In moderate to severe acute pancreatitis requiring interventions, NS was necessary for most patients, even in the initial course of the disease, then over a more prolonged period. Although EN was the first choice of NS, the need for PN or the combination of EN and PN was not neglectable. NS was continued after patient discharge in one-fourth of the patients with most EN.

- P02 -

ACCURACY OF PANCREATIC NEUROENDOCRINE NEOPLASMS GRADING BY ENDOSCOPIC ULTRA-SOUND-GUIDED FINE NEEDLE BIOPSY. G. Henry (1), R. Garces-Duran (2), L. Monino (2), T. Aouattah (2), D. Hoton (3), P. Baldin (3), C. Hubert (4), B. Navez (4), I. Borbath (2) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Gastroenterology, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Gastroenterology, [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Pathology, [4] Cliniques universitaires Saint-Luc, Brussels, Belgium, Surgery.

Introduction: Pancreatic neuroendocrine neoplasms (pNEN) are rare; their incidence was estimated at 1/100 000 people but is increasing in the last decades (2-5/100 000). pNENs represent 1-3% of all pancreatic tumours. The diagnosis is usually made by Endoscopic ultrasound (EUS). The WHO classification classifies NEN grading according to the Ki67 labelling index Ki67-LI). Grade 1 (G1) pNENs are defined by a Ki67-LI <3%, grade 2 (G2) by a Ki67-LI ranging between 3-20% and grade 3 (G3) by a Ki67- LI >20%. For many years the diagnosis was made by endoscopic ultrasound-guided

fine needle aspiration (EUS-FNA) with an accuracy at 90% [1]. However, we and others found that EUS-FNA often undergrades pNENs, mostly the G2 grade [2]. Recently authors showed a stronger correlation for Ki-67 values obtained by EUS and Fine needle Biopsy (FNB) and surgical specimens, and that EUS-FNB outperformed EUS-FNA in the evaluation of small pNETS [3].
Aim: We wanted to compare the grading of pNENS obtained by EUS-FNB with that obtained by surgery and to assess its adequacy, to externally validate results obtained by other teams.
Methods: We collected data of patients diagnosed with a pNEN between 2013 and 2022. For each patient we collected demographic data (DOB, gender, symptoms,…), data about the EUS (Needle used, tumour location and size, number of passages for the biopsy/aspiration and the pathology report), treatment, mainly if they underwent surgery, and pathological report. All data were brought together in a RedCAP.
Results: Thirty-seven patients had an EUS+FNA/B during the period; 54% where male. Mean age was 60.5 +/- 16 years. Thirteen % of the patients had a genetic predisposition condition. The main location was in the head of the pancreas (48.6%) with an average size of 25 +/- 29 mm. Out of the 37 patients, 17 (45.9%) underwent a surgery. Among patients who had EUS-FNA, 11 patients were operated (Table1).Overall, results show very poor correlation between FNA and surgery results. Among patients who had EUS-FNB, 6 were operated (Table 2). Although numbers are small, a much better correlation trend was observed, with only 1/6 mismatch between FNB and surgery (G2 by FNB being a G3 at final pathology). Table 1: Grading EUS-FNA VS Surgery Grade FNA Grade Surgery 1 2 3 Total 1 0 3 1 4 2 1 2 3 6 3 0 1 0 1 Total 1 6 4 11 Table 2: Grading EUS-FNB VS Surgery Grade FNB Grade Surgery 1 2 3 Total 1 1 0 0 1 2 0 2 1 3 3 0 0 2 2 Total 1 2 3 6
Conclusions: Due to the small size of our cohort, we were not able to perform statistical analysis with enough power. Nevertheless in a purely descriptive way we can see that the concordance between the EUS-FNB grading and the surgery seems to be more accurate than with EUS-FNA. We want to confirm these early findings in a bigger multicentric national cohort, taking advantage of the DNET registry run by the BGDO. 1. Weynand B, Borbath I, Bernard V, et al. Pancreatic neuroendocrine tumour grading on endoscopic ultrasound-guided fine needle aspiration: high reproducibility and inter-observer agreement of the Ki-67 labelling index. Cytopathology 2014;25(6):389-95. 2. Boutsen L, Jouret-Mourin A, Borbath I, et al. Accuracy of Pancreatic Neuroendocrine Tumour Grading by Endoscopic Ultrasound-Guided Fine Needle Aspiration: Analysis of a Large Cohort and Perspectives for Improvement. Neuroendocrinology 2018;106(2):158-166. 3. Crino SF, Ammendola S, Meneghetti A, et al. Comparison between EUS-guided fine-needle aspiration cytology and EUS-guided fine-needle biopsy histology for the evaluation of pancreatic neuroendocrine tumors. Pancreatology 2021;21(2):443-450.

- P03 -

PANCREATIC INTRADUCTAL TUBULOPAPILLARY NEOPLASM WITH ASSOCIATED INVASIVE CARCINOMA: A RARE PANCREATIC CYSTIC TUMOR WITH ENIGMATIC PATHOGENESIS. J. Fallas (1), M. Arvanitakis (2), J.-L. Van Laethem (2), M. Pezzullo (3), S. Debroux (4), J. Navez (5), J. Closset (5), P. Loi (5), C. Maris (6), N. D'Haene (1), L. Verset (1) / [1] Hopitaux Universitaires de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Belgium, Department of Pathology, [2] Hopitaux Universitaires de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Belgium, Department of Gastroenterology, Hepatology and Digestive Oncology, [3] Hopitaux Universitaires de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Belgium, Department of Radiology, [4] Chirec delta, Auderghem, Belgium, Department of Gastroenterology, [5] Hopitaux Universitaires de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Belgium, Department of Digestive Surgery, [6] Centre Universitaire Inter Régional d'Expertise en Anatomie Pathologique Hospitalière (CurePath), Charleroi, Belgium, Department of Pathology.

Case presentation: A 58-year-old patient presented with asthenia and mild epigastric discomfort. He reported recent weight loss of 20 kilograms, attributed to dietary changes following a newly diagnosed insulin resistance related to mild obesity. A familial history of pancreatic neoplasms affecting a brother, cousin and nephew prompted a CT-scan, revealing a 20 cm cystic and solid lesion originating from the body of the pancreas. Blood analysis indicated normal hepatic function. Ca19-9 and CEA tumor markers were within normal ranges. An endoscopic procedure with trans gastric fine needle aspiration confirmed the neoplastic nature of the lesion, while also unveiling the infiltration of the gastric mucosa by the tumor. Given the absence of distant lesions, the medical team opted for a distal pancreatectomy with splenectomy and subtotal gastrectomy. Gross examination showed a lesion comprising two large cysts, containing a hemorrhagic necrotic material and displaying extensive nodular and papillary formations within their lumens. Additionally, a poorly circumscribed whitish, solid to spongy, mass was observed, originating from the cysts, infiltrating the pancreatic parenchyma and penetrating the entire thickness of the stomach wall. Microscopic examination revealed extensive intraductal proliferations showing a pattern of alternating papillae and nodules of back-to-back tubular glands, forming cribriform sheets. These structures were lined by even cuboidal cells with an eosinophilic to amphophilic cytoplasm. The nuclei appeared small, round to oval, with inconspicuous nucleoli and exhibited minimal atypia. Additionally, a poorly differentiated infiltrating component was observed and characterised by small angulated nonmucinous glands embedded in a desmoplastic reaction. Immunohistochemical analysis revealed diffuse positivity for cytokeratin 7 and 19, along with diffuse expression of EMA (MUC1) but heterogeneous MUC6 positivity. Tumor cells were negative for

MUC2 and MUC5AC. P53 expression was wild-type. TRK immunohistochemistry was negative, and no evidence of microsatellite instability was found. Next-Generation Sequencing identified two variants of undetermined biological and clinical significance in the POLE (POLE p.R2149C) and ALK (ALK p.G922R) genes. No known pathogenic mutations nor fusion genes were detected. We concluded with the diagnosis of intraductal tubulopapillary neoplasm with associated invasive poorly differentiated adenocarcinoma. Given the presence of lymph node metastases, neoadjuvant chemotherapy was started, and genetic testing was recommended considering the extensive family history of pancreatic cancer.
Discussion: Intraductal tubulopapillary neoplasms (ITPN) represent a rare subset of cystic neoplasms of the pancreas, accounting for 3% of all intraductal neoplasms and less than 1% of pancreatic epithelial neoplasms. This entity is characterised by ductular differentiation, forming tubes and papillae, and notably lacking mucin production. Associated invasive carcinoma is found in around 70% of cases. The genetic profile of ITPNs differs markedly from that observed in ductal adenocarcinomas and other intraductal neoplasms of the pancreas, lacking the typical KRAS mutation. ITPNs are also associated with a significantly more favorable prognosis; even in cases of ITPNs with associated invasive carcinoma, the overall 5-year survival rate is close to 70%. This case highlights the importance of considering ITPN as a differential diagnosis for pancreatic cystic tumors. It also emphasizes the need for continued investigation of mutational profiles to gain deeper insights into the pathogenic mechanisms underlying this distinctive entity.

- P04 -

A RARE MANIFESTATION OF CHRONIC PANCREATITIS: PANCREATIC PANNICULITIS, FROM DIAGNOSIS TO MANAGEMENT. A. Pavlidi (1), A. Hadefi (2), M. Arvanitakis (2) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, [2] Erasme Hospital, Brussels, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology.

Pancreatic panniculitis is a rare skin manifestation, affecting 2-3% of all patients with underlying pancreatic disease, mostly associated with acute or chronic pancreatitis. It is characterized by inflammation of the subcutaneous fat due to massive release of pancreatic lipolytic enzymes into the circulation and thus allowing lipase and amylase to penetrate the adipose tissue causing saponification of subcutaneous fat. It remains as one of the most challenging areas for clinicians since the nodules of pancreatic panniculitis can mimic other forms of panniculitis or even other skin conditions and can precede findings of a pancreatic disease up to 40% of the cases. If clinical suspicion, skin biopsy remains the gold standard for diagnosis with ghost adipocytes as pathognomonic finding. Its treatment, clinical course and prognosis are usually related with the pancreatic disease.
Case Report: We report the case of a 65-year-old man with a past medical history of decompensated alcoholic liver cirrhosis complicated by portal hypertension and septic portal vein thrombosis who was admitted to the hospital initially with a functional acute kidney failure. During his hospitalization, the patient started having fever spikes and elevated CRP levels without any pathogen identification. He had very high serum lipase levels and elevated lipase level in ascites fluid without any associated abdominal pain. An abdominal CT scan was performed which demonstrated an obstructive calcification in the setting of chronica calcifying pancreatitis. In the days that followed, the patient presented with multiple erythematous-purplish, painful nodules in both lower extremities for which the biopsy was in favor of pancreatic panniculitis. A pancreatic fistula was suspected due to the portal vein thrombosis and elevated lipase in the ascitic fluid but diagnosis could not be concluded neither after the abdominal CT nor after the magnetic resonance imaging (MRI) because of the presence of the voluminous ascites. The patient had a favorable clinical and biochemical outcome rapidly after the administration of one only subcutaneous injection of octreotide and skin lesions regression. One month after, he had a new elective admission for Endoscopic Retrograde Cholangiopancreatography (ERCP) following extracorporeal shock wave lithotripsy (ESWL) for pancreatic duct drainage during which partial stone extraction was achieved and a pancreatic stenting was inserted. Unfortunately, the patient died 13 days after his last admission because of systemic infection despite large spectrum antibiotics, leading to an acute-on-chronic liver failure.
This case highlights the importance of early clinical suspicion of pancreatic panniculitis where pancreatic disease must be considered even in asymptomatic patients. In some cases, pancreatic panniculitis can indicate the exacerbation of a chronic condition, while in other cases it can lead to the early detection of a hidden pancreatic carcinoma. Certainly, from diagnosis until treatment, this requires a multidisciplinary approach with close cooperation between the different specializations: gastroenterology, radiology, dermatology, pathology and oncology if needed.

- R01 -

NEUROENDOCRINE TUMORS IN THE STOMACH: AN EPIDEMIOLOGICAL ANALYSIS OF BELGIAN CANCER REGISTRY DATA. M. Maly (1), E. Callebout (1), A. Hoorens (2), S. Ribeiro (1), K. Geboes (1) / [1] Universitair ziekenhuis Gent, Belgium, Gastroenterology, [2] Universitair ziekenhuis Gent, Belgium, Pathology.

Introduction: Gastroenteropancreatic neuroendocrine neoplasms (GEP-NEN) are rare and heterogenous tumors with a variable clinical presentation. According to the WHO 2022 guidelines GEP-NEN include neuroendocrine tumors (NETs), neuroendocrine carcinomas (NEC) and mixed neuroendocrine and non-neuroendocrine neoplasms (MiNEN). NETs are classified as low grade (grade 1 or G1), intermediate grade (grade 2 or G2) or high grade (grade 3 or G3), based on mitotic activity and Ki-67 index. NECs are always high grade (G3). Neuroendocrine tumors of the stomach (gNEN) in addition should be clinically subtyped as this has therapeutic implications. Type 1 and type 2 gNET are ECL-cell NET driven by hypergastrinemia, most often due to atrophic corpus gastritis (type 1), rarely due to a Zollinger-Ellison syndrome (type 2). Type 3 is a rare and sporadic NET. In character, type 1 gNET are relatively innocuous while type 3 gNET are biologically more aggressive. Large (inter)national or population-wide cohorts are hardly available for gNEN.
Aim: The aim of this research project was to map the epidemiology of gNEN in Belgium, with specific attention to the distribution of demographic and clinical characteristics of gNEN. In addition, quality and evolution of histology reports were assessed.
Methods: This research project concerns a national cohort study on the epidemiology of gNEN in Belgium over the period 2010-2019, analyzing patient data obtained through the Belgian Cancer Registry (BCR). The data can be considered complete for the Belgian population, given health insurance is mandatory for all inhabitants. Pathology reports of all gNEN diagnoses were manually evaluated by the investigators and reclassified according to the most recent WHO 2022 guidelines.
Results: 894 gNEN were diagnosed in 605 patients in Belgium over the period 2010-2019, corresponding to an annual age-adjusted incidence of 0.67 per 100,000 persons per year. In some patients, multiple NETs were diagnosed at the same time or during follow-up. The median age at diagnosis was 64 years and there was a slight female predominance (54.1%). The proportion of NEC was 14.7% which corresponds to an age-adjusted incidence of 0.11 per 100,000 persons per year, with a median age of 71 years and a large male predominance (71.3%). MiNEN were diagnosed in 36 patients (3.9%). Concerning gNETs, G1 NETs appeared most prevalent (57.4%) followed by G2 (22.5%) and G3 NETs (2.0%). In only 3.8% the clinical subtype was explicitly stated in the histology report, in the remaining cases the investigators made a deduction based on the available data. Type 1 tumors were diagnosed in 70.5% of cases, type 3 tumors in 14.4% and a markedly lower prevalence of type 2 tumors (0.45%) was seen. In only 37.3% of all considered type 1 NETs, ECL-cell hyperplasia was explicitly mentioned in the pathology report. In the setting of atrophic gastritis however, ECL-cell hyperplasia (particularly the micronodular type), is a diagnostic feature of corporal autoimmune atrophic gastritis. The majority of type 1 tumors were classified as low of intermediate grade; respectively 56% G1, 31.6% G2 and 7.5% NETs without possible differentiation between G1 or G2. For type 3 tumors however, there was no strong correlation with a high grade (with respectively 36.4% G1, 24.8% G2 and 5.0% G3 NETs). A favourable evolution in reporting the degree of proliferation and differentiation by pathologists has been observed over the years. In 2019, the Ki-67 index was reported in 92.2%, the mitotic rate in 81.3% and the grade of differentiation in 82.3% of patients while these figures were only just above 50% at the start of registration. Metastatic or stage IV tumors were diagnosed in 15.4% of patients with gNEN and in 50% of patients with MiNEN. Almost 65% of all NECs were metastasized.
Conclusions: 605 patients were diagnosed with gNEN in Belgium over the period 2010-2019, with an annual age-adjusted incidence of 0.67 per 100,000 persons per year. Other large (inter)national cohorts to compare with our data were not found. Therefore multicenter, preferably population-wide prospective studies are needed to better map the epidemiology and clinical characteristics of gNEN in Europe and worldwide. In only 3.8% the clinical subtype was explicitly stated in the histology report. This emphasizes the importance of standardized and evidence based datasets for the pathology reporting of NENs.

- R02 -

GASTROINTESTINAL COMPLICATIONS IN A LEUKEMIC CHILD: ADENOVIRUS CHALLENGES POST-TRANSPLANT. M. Racu (1), P. Mazilier (2), L. Kornreich (2), P. Calò (2), L. Verset (1) / [1] CHU Brugmann, Brussels, Belgium, Pathology, [2] HUDERF, Brussels, Belgium, Pediatric Hemato-Oncology.

The evaluation of gastrointestinal specimens in immunosuppressed patients can be challenging due to a spectrum of pathologies resulting from treatment-related complications or a diverse range of pathogens and opportunistic agents.
Case Report: To illustrate this complexity, we present the case of a 9-year-old boy with B-acute lymphoblastic leukemia diagnosed in August 2020 and put into complete remission with a first line treatment according to the EORTC 58081 protocol. In January 2023, an early isolated extramedullary relapse in the testis occurred and second complete remission

was achieved with a treatment according to the IntreALL 2020 protocol. The child underwent hematopoietic stem cell transplant (HSCT) after receiving a conditioning regimen with total body irradiation with testicular boost and high-dose etoposide. He received a large immunosuppressive therapy of graft-versus-host prophylaxis (thymoglobulines, ciclosporine and post-transplant methotrexate). During post-transplant hospitalization, the child encountered several infectious complications. Notably, 21 days after transplant, he suffered from profuse watery diarrhea. To exclude acute graft-versus-host disease, a gastrocolonoscopy was conducted, revealing signs of oesophagitis and rectal oedema, while the rest appeared unremarkable. Oesophageal, gastric, duodenal, and right colon biopsies showed no significant alterations. However, the glands of the rest of the colon and rectum biopsies focally exhibited signs of viral infection characterised by multinucleated cells with ground-glass appearance. The architecture of the epithelium was preserved and there was no significant inflammation. There was no evidence of graft-versus-host disease. Immunohistochemistry was negative for Cytomegalovirus but came back positive for Adenovirus. Adenovirus infection was confirmed by PCR on the colon biopsy (maximum viral titre of 450.795.000 UI/mL) and on the weekly plasmatic monitoring (maximum viral titre of 287.392 UI/ml). The child was treated with antiviral therapy based on weekly cidofovir. The infection was promptly controlled and blood viremia was negativized without the need of cytotoxic T lymphocyte therapy. Unfortunately, primary graft failure was diagnosed 31 days after transplant, partially attributed to the viral toxicity of viremia/adenovirus colitis. Screening blood PCR for adenovirus before HSCT was negative. Adenoviruses are non-enveloped icosahedral DNA viruses from the Adenoviridae family present in most vertebrates. They are ubiquitous and commonly found in the respiratory tract and stool of children. While immunocompetent individuals usually experience mild, self-limiting disease, adenovirus infection can be life-threatening in immunocompromised children, with mortality rates ranging from 50-80%, regardless of the site of infection. In immunocompromised patients, diarrhea is the most common manifestation, but gastrointestinal disease can vary from mild diarrhea to haemorrhagic colitis. Clinical presentations may also include fever, interstitial pneumonitis, hepatitis, ascending cholangiohepatitis, haemorrhagic cystitis, nephritis, central nervous system disease or disseminated disease. The incidence of adenovirus infection following HSCT has increased in the recent years and the frequency is higher in pediatric population. This is attributed to various factors, such as greater awareness of this pathogen, the aggressiveness of conditioning regimens, greater sensitivity of diagnostic methods and systematic screening. The occurrence of infectious complications during engraftment period can dramatically compromise the success of HSCT. Therefore, early detection and treatment of pathogens such as adenovirus remain crucial.

- R03 -

SWEET'S SYNDROME WITH GASTRO-INTESTINAL INVOLVEMENT. N. Greiner (1), H. Dano (2), F. Etogo-Asse (3), B. Alexandre (4), O. Dewit (1) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Gastroenterology and hepatology, [2] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Anatomo-pathology, [3] Clinique Saint-Jean, Brussels, Belgium, Gastroenterology and hepatology, [4] CHR, Namur, Belgium, Gastro-enterology and hepatology.

Sweet's syndrome, also known as "acute febrile neutrophilic dermatosis", is characterized by the abrupt onset of painful erythematous plaques or nodules, associated with fever, elevated neutrophil count and response to corticotherapy. Although Sweet's syndrome is known to be associated with several gastrointestinal conditions, notably with gastrointestinal infections, as well as with inflammatory bowel disease, primary gastrointestinal involvement is much more rarely described and poses significant diagnostic challenges. To our knowledge, there are only four cases reported in the literature to date.
Case Report: We present a particularly severe case of a 30-year-old male without significant medical history who presented to the emergency department with abdominal pain for 7 days, followed by the apparition of melaena, polyarthralgia and the development of painful, erythematous, crateriform skin lesions. Cutaneous Sweet's syndrome was confirmed by skin biopsies. Abdominal CT-scan revealed proximal jejunitis and ileitis, interspersed with areas of normal bowel. Endoscopic examinations confirmed severe involvement of the entire small intestine, but first pathology results showed only mild and unspecific inflammation. All infectious samples were negative. Multiple stool and blood investigations were inconclusive. Evolution was rapidly dramatic with major weight loss, development of severe hypoalbuminemia (18 g/dl), hemorrhagic shock requiring uptake in the intensive care unit. Colchicine and broad spectrum antibiotics yielded no improvement. Review of the pathological samples revealed an inflammatory infiltrate rich in neutrophils associated with a perivascular neutrophilic infiltrate, with leukocytoclasia and some eosinophils. There was no vasculitis. These histological characteristics were similar to those of cutaneous Sweet's syndrome, and consistent with the other cases of gastro-intestinal Sweet's syndrome described in the literature. Corticosteroid therapy was initiated. Under this treatment, the patient experienced fast and complete clinical improvement. After 3 months, corticosteroid therapy was discontinued, without other maintenance treatment. To date, 15 months later, the patient has shown no signs of relapse.

- R04 -

DRUG-INDUCED OESOPHAGITIS MIMICKING OESOPHAGEAL NEOPLASIA. K. Ferdinande (1), D. Tate (2), T. Lobaton (2), L. Ferdinande (3), A. Hoorens (3), P. Hindryckx (2) / [1] Ghent University Hospital, Ghent, Belgium,

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Case description: An 80-year-old man presented with haematemesis, anorexia, retrosternal chest pain, dysphagia and unspecified weight loss. The patient had a cardiovascular history of ischaemic heart disease and peripheral vascular disease. His current medication included acetylcysteine, bisoprolol, perindopril, amlodipine, atorvastatin, edoxaban, bumetanide, moxonidine and spironolactone. Clinical examination showed a soft and non-tender abdomen. His vital signs were normal. Laboratory tests were significant for haemoglobin 11.8 g/dL, CRP 92.8 mg/L, leukocyte count 9.78 x10E3/µL and a lactate 3.21 mmol/L. Cross-sectional imaging revealed an eccentric oesophageal tumour on the left at carina level with severe narrowing of the lumen and upstream dilatation. An active contrast blush was seen in the centre of this mass in the venous phase. Additionally, extensive infiltration of the surrounding fatty tissue was seen. An oesophagogastroduodenoscopy (OGD) was performed and showed a bulky tumoral lesion starting mid-oesophageal over a length of 15 cm distally, highly suspicious of malignancy. The lesions caused significant obliteration of the esophageal lumen, just passable with a standard gastroscope. Venous oozing of the lesion was confirmed and hemostasis was achieved by local application of haemostatic powder. The patient was re-scheduled for a second-look gastroscopy the other day, for histopathological confirmation of malignancy. This second OGD showed a completely different picture. Multiple very deep ulcerations were seen, with the impression of a fistula. Large blood clot formation adherent to the ulcerations was. This endoscopic image was far less suspicious for a primary oesophageal neoplasia. Biopsies were taken carefully at the margin of the ulcerative zone. The tissue was very fragile with spontaneous oozing requiring application of hemostatic gel. Histopathological examination demonstrated an ulcerative oesophagitis with several fragments consisting of an inflammatory exudate with polarizable foreign material, consistent with severe pill-related oesophagitis. The surrounding epithelium showed spongiosis (dialted intercellular spaces) and neurophilic infiltration. There was no evidence of malignancy. The patient was treated conservatively with short-term high-dose proton pump inhibitors (PPIs). We also instructed the patient with preventive measures to protect the esophagus from further injury. Repeat endoscopies (after 5 days and after 6 weeks) showed progressive mucosal healing and biopsies were reassuring. The presumed diagnosis of a pill-induced oesophagits could be confirmed.
Discussion: Pill induced oesophagitis is a well described but underreported oesophageal mucosal injury caused by a direct toxic effect on the oesophageal mucosa by the culprit medication (1,4). The most common culprits are antibiotics, non-steroidal anti-inflammatory medications and bisphosphonates (1-4). In our case, aspirin or blood pressure-lowering drugs were most likely the responsible for this pill-induced oesophagitis (1-4). However, any drug can trigger pill-induced oesophagitis in the presence of patient-related factors that cause prolonged transit time of mediation in the oesophagus (1). In our case, patient-related factors (older age, lower saliva production, inadequate intake of medication, inadequate water intake, etc..) could have contributed to the event, but obvious anatomic or underlying motility disorders of the oesophagus were absent. The most common symptoms of pill-induced esophagitis are odynophagia, dysphagia and retrosternal chest pain (1-3). More severe symptoms include a presentation with gastrointestinal haemorrhage, and less frequently a presentation with oesophageal perforation (1-4). In our case, the patient presented with acute upper gastrointestinal haemorrhage, indicating a more severe presentation. Upper gastrointestinal endoscopy is the gold standard for the evaluation of pill induced oesophagitis (1). The classicaly endoscopically presentation is inflammation and ulceration at the proximal and middle third of the oesophagus (3-4). Biopsies usually show nonspecific oesophagitis with erosions, ulcers, active inflammation with neutrophils and occasionally eosinophils, surface epithelial damage and granulation tissue. When present, polarizable material may be an important diagnostic clue. Pill induced oesophagitis has an excellent prognosis and is a self-limiting disorder following supportive treatment (1-4). If possible, discontinuation and prescribtion of alternative drugs are recommended (1,4). Short-term treatment with PPIs are also recommended in the management of pill induced oesophagtis (1).
Conclusion: This case calls attention to include pill induced oesophagitis in the differential diagnosis in patients presenting with odynophagia, dysphagia, retrosternal chest pain and potentially upper GI bleeding. The cornerstone is to exclude other diagnosis like oesophageal malignancy with upper GI endoscopy and histopathological examination. Pill induced oesophagitis has an excellent prognosis following conservative treatments, as demonstrated in our case with complete resolution of the initial severe presentation.

- R05 -

IMMATURE SQUAMOUS METAPLASIA OF ESOPHAGEAL GLANDS ASSOCIATED WITH SQUAMOUS CELL CARCINOMA: A POTENTIAL PITFALL IN ESD SPECIMEN.

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Introduction: The management of superficial esophageal squamous cell carcinoma (eSCC) has evolved with minimally invasive surgical techniques like endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD).

Currently, ESD is the primary choice for managing superficial eSCC. However, immature squamous metaplasia (ISM) in the esophagus and its potential role as background for the development of neoplastic lesion is poorly characterized compared to its counterpart in the cervix. This case reports an ESD resection, highlighting ISM lesions associated with eSCC.

Case Presentation: A 58-year-old male underwent ESD for a 26 mm superficial esophageal lesion. Macroscopic examination revealed a poorly circumscribed, erythematous, ulcerated lesion. Microscopic analysis disclosed poorly differentiated eSCC associated with extensive ISM without deep and lateral margin involvement. ISM lesions in the lamina propria exhibited multilayered immature squamous cells with a cystic appearance and a ductal pattern, suggesting an origin from ducts. ISM lesion were found in the lamina propria and was characterized as multilayered immature squamous cells organised in islets with a cystic appearance and lined by columnar and mucus-secreting epithelial cells. Increased nucleocytoplasmic ratio with somes slight atypia were found and some mitoses were seen on the basal layer only. The ductal pattern of the lesion suggests that they emerged from ducts and extends to the surface. PAS-diastase staining and immunostaining was completed to characterized the origins of the ISM. The lesion was immunoreactive to P63 contrasting with the negativity in mucus-secreting cells while PAS-diastase staining revealed the presence of mucus without goblet cells. Ki-67 demonstrated proliferating cells limited in basal and parabasal compartments. Duct draining submucosal glands displayed p63 positivity and PAS-diastase negative cells while the submucosal glands was lined by PAS-diastase positive cells. Ber-EP4 was positive in ISM lesion. In contract, the eSCC exhibited solid nests with severe atypia, classified as pT1b. Immunostaining show a negative Ber-EP4 staining, diffuse p63 reactivity, and disrupted basal membrane as confirmed by collagen IV immunostaining indicated invasive characteristics.

Discussion: This case revealed ISM originating from esophageal gland ducts alongside poorly differentiated eSCC. Two types of glands exist in the esophagus, cardiac-type glands in the lamina propria and submucosal glands draining into the muscularis mucosae. Early stratification of ductal epithelium and exclusive mucus secretion in the lamina propria provide suspicion of ISM's origin from esophageal cardiac-type glands in our case. Correlated with previous studies, it is postulated that esophageal ISM may derive from gland stem cells, capable of generating both squamous and Barrett's columnar cells. Immunohistochemistry, particulary Ber-EP4, plays a pivotal role in differentiating ISM from invasive lesions. Ber-EP4's reactivity in immature, metaplastic, and dysplastic conditions, including ISM, provides a crucial diagnostic tool. The nuanced classification of esophageal ISM as preneoplastic or dysplastic underscores the importance of precise recognition to prevent misinterpretation. The observed association between ISM and eSCC is currently unclear and need further investigation. The distinction of esophageal ISM and invasive cancer or eSCC spreading to the submucosa is a major challenge and immunohistochemical features coupled with the preservation of the basal membrane confirmed that the esophageal ISM is a distinct entity wich need to be known to be recognised in clinical practice to prevent misinterpretation and a over-managing of the lesion. These elements light the necessity of additional research to establish a comprehensive understanding of the relationship between ISM and eSCC and to determine the role of ISM for precise classification and recognition in the esophagus.

Reference: Immature squamous metaplasia of esophageal glands associated with squamous cell carcinoma. Verset L, Huberty V, Bourgeois V, Lemmers A, Demetter P. Acta Gastroenterol Belg. 2022 Apr-Jun;85(2):396-399. doi: 10.51821/85.2.8316.

- R06 -

AN UNCOMMON TUMOUR OF THE OESOPHAGUS. H. Lauwers (1), M. De Maat (2), P. Dewint (3), S. Bouhadan (3), A. Driessen (1) / [1] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Pathologie, [2] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Abdominale, Kinder- en Plastische Heelkunde, [3] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastro-enterologie en hepatologie.

Oesophageal cancer is the 7th most common cancer with a high mortality rate as it is the 6th leading cause of cancer-related death worldwide. Worldwide squamous cell carcinoma is the most prevalent histological type of cancer. However in the oesophagus there is a change in histological type in time. Whereas in the mid-twentieth century squamous cell carcinoma was the most prevalent type, nowadays the majority of oesophageal carcinomas is the adenocarcinoma. The squamous cell type carcinoma, of which the incidence is significantly declining, presents mostly in advanced stage. It is most commonly situated mid-oesophagus. Besides the classical squamous cell type carcinoma, there are different but very rare subtypes.

Case Report: We present a case of a 60-year old male, who was referred to the gastroenterologist because of a significant problem of dysphagia. Patient was known with a medical history of alcohol abuse in the past. Endoscopic examination revealed a large papillomatous lesion in the oesophagus. Despite using a paediatric endoscope it was not possible to pass the lesion, pointing to a significant narrowing of the oesophagus. These features suggest a malignant process. However despite recurrent endoscopic examination and sampling, the morphological features on biopsy (well-differentiated lesion with no cytological atypia and no signs of invasion) did not suggest malignancy. As a malignant lesion could not be excluded due to the persistence of the symptoms and the endoscopic findings, the patient underwent an oesophagectomy, revealing a large papillary tumour. Microscopic examination showed a well-differentiated squamous tumour, corresponding to a verrucous carcinoma.

A verrucous carcinoma is an uncommon subtype of squamous cell carcinoma, occurring not only in the oesophagus, but also in other areas such as oropharynx, larynx and genitalia. The verrucous appearance of the tumour with hyperkeratosis and parakeratosis hampers its diagnosis on endoscopic biopsies as only the superficial part of the lesion without the stroma can be examined. Moreover the absence of cytological atypia makes its diagnosis even more difficult. As a result of its delay in diagnosis the tumour may present in an advanced stage, resulting in a poor prognosis.

- R07 -

A PATIENT WITH GASTRIC OUTLET SYNDROME DUE TO MULTIPLE POLYPS IN THE STOMACH. A. Kerckhofs (1), E. Macken (2), G. Hubens (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, Abdominal Surgery.

Gastric polyps, which are diagnosed in approximately 6 % of the upper gastrointestinal endoscopies, are most commonly incidental findings. The origin of these polyps is heterogeneous, varying from the surface epithelium, the glandular epithelium, stromal or lymphoid tissue. Most polyps have characteristic features such as their localisation, the endoscopic appearance and the appearance of the surrounding gastric mucosa. The majority of polyps are benign, e.g. fundic cystic gland polyps and hyperplastic polyps. The adenomatous polyps however are neoplastic, and require a thorough follow-up to exclude an associated malignant tumour. Rarer polyps, such as hamartomatous polyps, also exist.
Case Report: We present a case of a 57-year-old man who was referred to our hospital with symptoms of vomiting and dysphagia. His medical history shows a partial gastrectomy in another centre five years ago. Two months before, he was already admitted because of intermittent bleeding of the gastric pouch. Because of the current symptoms pointing to passage obstruction, this patient underwent an explorative laparotomy with resection of the gastric pouch and the oesophagojejunostomy. Gross examination of the specimen reveals the presence of numerous polyps of the mucosa. The mucosa was completely altered with copious polyps varying in dimensions up to two to three centimetres. Microscopically, the polyps were composed of irregularly dilated and elongated glandular serrated foveolar structures delineated by a hyperplastic mucosal epithelium. The lamina propria was oedematous and contained a diffusely increased mixed inflammatory infiltrate. The morphological features of these polyps resembled hyperplastic polyps. Further clinical examination revealed that our patient was known with the Cronkhite-Canada syndrome, an uncommon non-congenital disorder with no known aetiology. In addition to multiple gastrointestinal polyps, the disease is associated with other ectodermal alterations, as was the case in our patient, such as atrophic nail changes, mild alopecia and palmar hyperpigmentation. Based on the features in this patient, hamartomatous polyps were diagnosed.
The morphological features of this gastrointestinal polyposis syndrome are not specific on itself and may resemble other types of polyps such as inflammatory polyps or hyperplastic polyps. Hence, information on clinical features unrelated to the gastrointestinal tract is crucial to make an adequate histological examination of these polyps. This case underscores the imperative consideration of rare syndromes in the differential diagnosis of gastro-intestinal polyps.

- R08 -

DIAGNOSTIC PITFALL IN THE GASTRIC MUCOSAE. H. Dano (1), L. Navez (2), C. Van der Pluijm (3), A. Mourin (4), P. Deprez (5), L. Libbrecht (6) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Anatomo-pathology, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Pathology, [3] Cliniques de l'Europe Site Sainte-Elisabeth, Uccle, Belgium, Gastroenterology, [4] Institut de Pathologie et de Génétique, Charleroi, Belgium, Pathology, [5] Cliniques universitaires Saint-Luc, Brussels, Belgium, Gastroenterology, [6] AZ Groeninge, Kortrijk, Belgium, Pathology.

Introduction: Sometimes non-neoplastic changes of the gastric mucosa mimic diffuse-type gastric carcinoma, specifically signet-ring cell adenocarcinoma (SRCA). In fact, gastric epithelial cells undergoing signet-ring cell change (SRCC) have a cellular morphology that is almost identical to SRCA, often leading to misdiagnosis. Accurate recognition of SRCC is essential to avoid overdiagnosis and overtreatment of SRCA. Research on this topic is limited and clinicians lack formal diagnostic tools when signet-ring cells (SRC) are detected in biopsy specimens.
Aim: The aims of this study are threefold. Firstly, to increase the awareness of both clinicians and pathologists of this rare but highly significant entity. Secondly, to report four additional cases of SRCC and analyse them alongside SRCA to compare their morphological and phenotypic features and their evolution over time. Finally, to highlight the potential utility of endoscopic resection to confirm the diagnosis.
Methods: Morphological differentiation from SRCA based on histological and immunohistochemical profiles seems to allow better discrimination.
Results: Cells in SRCC strongly express E-cadherin, show weak and heterogeneous p53 expression, and have a low Ki-67 index. In contrast, cells in SRCA strongly express p53, have high proliferation rates, and show either no or weak E-cadherin staining. Genetic analysis may be useful in identifying patients at risk of hereditary early diffuse gastric adenocarcinoma (HDGC), which can mimic SRCC.

Conclusions: In conclusion, the finding of SRC in gastric biopsies should prompt the clinician to rule out SRCA. Particular attention should be paid to histological and immunohistochemical analysis of cell and tissue architecture. SRCC, which often occurs in an inflammatory or ischaemic setting, is a rare non-neoplastic phenomenon that morphologically closely resembles SRCA. Suspicion for SRCC should be raised when cells are non-atypical, lack typical malignant marker expression and are located superficially in the lamina propria. As shown in patient 2, SRCC can remain in the stomach for a long time without progression. Endoscopic resection could potentially become a valuable diagnostic tool. We highlight the lack of diagnostic tools to better differentiate these entities and emphasises the need for further research to allow early diagnosis before disease progression.