ABSTRACTS

35th Belgian Week of Gastroenterology 2023

ABSTRACTS

- A01 –

INSUFFICIENT KNOWLEDGE OF HEPATITIS B AND C VIRUS REACTIVATION AMONG SPECIALIST PHYSICIANS IN DUTCH-SPEAKING BELGIUM: THE CHOICE TRIAL (CHRONIC HEPATITIS B/C SCREENING IN PATIENTS ON IMMUNOSUPPRESSIVE THERAPY AND CHEMOTHERAPY)

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Introduction: Belgium is considered a low endemic area for hepatitis B and C virus (HBV and HCV) infections. However, HBV and HCV reactivations in chronically infected patients are an emerging problem because of the increasing use of cytotoxic or immunosuppressive therapy regimens. Although their clinical course may be mild, some patients develop a fulminant hepatitis or are prone to dose reduction or even discontinuation of treatment. Even though several scientific societies propose universal HBV screening before the start of cytotoxic or immunosuppressive therapy, HBV reactivation still occurs in daily practice. No recent surveys have been performed/published assessing HBV/HCV knowledge in specialists prescribing these medications.
Aim: Assessing knowledge and awareness regarding HBV/HCV reactivation among oncologists, gastroenterologists, rheumatologists, and dermatologists in Belgium. In addition, associations between survey scores and several variables will be studied.
Methods: A short questionnaire (Q) in Dutch was designed in duplicate using the REDCap software (i.e., Q1 for an oncologic and Q2 for a non-oncologic setting) assessing descriptive variables (i.e., discipline, subdiscipline (only applicable in Q1), years of experience, working in an academic center and having witnessed an HBV/HCV reactivation in their own practice) and nine content questions, of which four background and five clinically oriented. Of these five clinical questions, three were discipline-specific (specific for Q1 and Q2). The survey was disseminated by e-mail between 10/01/22 and 20/05/22 to 11 hospitals in Belgium (three university, eight non-university). Hepatologists and specialists working in both a university and a non-university hospital at the same time, were removed from the mailing list. In each center, a local ambassador supervised the survey dissemination and confirmed its receipt. Non-responders received up to two reminders. Statistical analysis was done using SPSS version 28.
Results: A total of 116 specialist physicians participated in this survey, including 64 oncologists (55.2%), 21 inflammatory bowel disease specialists (18.1%), 16 rheumatologists (13.8%), and 15 dermatologists (12.9%). Oncologists were further subspecialized in solid tumors (52.4%), hematology (33.3%), or digestive oncology (14.3%). A total of 33.6% of participants had less than 5 years of experience as specialist physician and 37.1% works in an academic center. As much as 28.4% of participants had already experienced an HBV reactivation in their own practice. Out of 116 survey responses, 104 were complete. Less than 30% of participants obtained a score above 50%. Mean overall scores (total, Q1, and Q2) were 36.2%, 33.7%, and 40.2% respectively. Mean scores for clinical questions (total, Q1, and Q2) were 48.6%, 44.4%, and 55.6% respectively. Mean overall scores for background and non-discipline-specific questions were 20.2% and 36.0% respectively. Scores were not influenced by years of experience, nor working in a university hospital. HBV/HCV prevalence in Belgium, clinical course of HCV reactivation, and timing of HBV/HCV prophylaxis were better known by gastroenterologists. They scored significantly better on non-discipline-specific questions ($p=0.009$). Moreover, oncologists that have already witnessed a hepatitis B reactivation in their own practice, are better aware of hepatitis B screening guidelines prior to administration of chemotherapy ($p=0.005$) and immunosuppression ($p=0.033$).
Conclusions: Knowledge of HBV/HCV reactivation is at present insufficient among specialist physicians, with differences according to specialty. Gastroenterologists scored better on non-discipline-specific questions (prevalence, clinical course, HBV reactivation prophylaxis), whereas oncologists are better aware of HBV screening guidelines, especially if they have witnessed a hepatitis B reactivation themselves. This also shows that creating awareness is feasible. Therefore, providing clear guidance and raising awareness among all physicians of the involved specialties is of paramount importance. National hepatology and oncology organizations can play an important role in this regard.

- A02 -

A NOVEL METHOD FOR THE QUANTIFICATION OF IMMUNOHISTOCHEMISTRY IN RELATION TO HEPATIC ZONATION AND CORRECTING FOR STEATOSIS. C. Peleman (1), W. De Vos (2), L. Van Nassauw (3), I. Pintelon (2), A. Driessen (4), A. Van Eyck (5), C. Van Steenkiste (5), L. Vonghia (5), J. De Man (5), B. De Winter (5), T. Vanden Berghe (6), S. Francque (5), W. Kwanten (5) / [1] University of Antwerp, Antwerp, Belgium, Medicine and Health Sciences, [2] University of Antwerp, Antwerp, Belgium, Laboratory of Cell Biology & Histology, Dept. Veterinary Sciences, [3] University of Antwerp, Antwerp, Belgium, Department of ASTARC, Faculty of Medicine and Health Sciences, [4] Antwerp University Hospital, Edegem, Belgium, Department of Pathology, [5] University of Antwerp, Antwerp, Belgium, Laboratory of Experimental Medicine and Pediatrics, Infla-Med Centre of Excellence, [6] University of Antwerp, Antwerp, Belgium, Laboratory of Pathophysiology.

Introduction: Immunohistochemistry (IHC) provides important information about the distribution of epitopes of interest in different zones of the liver lobule in health and disease. Results of IHC are mostly presented as qualitative descriptions with representative images or graded with a semi-quantitative scoring system, which may lack sensitivity to detect subtle changes. In addition, zonal distribution of IHC signals and alternations hereof, although potentially relevant, are not captured by current automated global quantifications due to the lack of anatomical delineation. Finally, in non-alcoholic fatty liver disease (NAFLD) the hepatocellular lipid-laden macrovacuoles represent a non-staining area confounding surface-based quantification of IHC.
Aim: We present a method to objectively quantify IHC staining patterns with regards to the relative distance across the liver lobule, and we compared distributions of two epitopes related to lipid peroxidation in normal versus steatotic livers.
Methods: Male C57BL/6J mice (n=6/group) were sacrificed after 4weeks on choline-deficient L-amino acid-defined high-fat diet (NASH) or standard diet (controls) and formalin-fixed paraffin-embedded liver tissue was collected. The CDAHFD is a known model to induce NASH. IHC was performed for two epitopes, i.e. lipid peroxidation breakdown product 4-hydroxynonenal (4-HNE, ab46545, USA) and the endogenous lipid peroxidation detoxification system glutathione peroxidase 4 (GPX4, ab125066, USA), both visualised with 3,3'-diaminobenzidine (DAB). After whole slide image acquisition with the Zeiss Axioscan 1, liver lobules were reconstructed in all subjects using a script for FIJI open-source image analysis freeware with the manually selected centrolobular veins acting as nuclei of inception. Next, after deconvolution of the IHC signal DAB pixel intensities were calculated as a function of the relative location (with respect to the central vein and the lobular edge) within a liver lobule. Binarization of pixels into positive or negative for 4-HNE and GPX4 IHC was performed using an arbitrary manual threshold grey value. A separate segmentation based on manual thresholding and filtering was performed to annotate the majority of lipid vacuoles to allow correction for steatosis. Data were processed in R Studio, using the additional package "dplyr" for grouped summary statistics.
Results: After 4 weeks of CDAHFD feeding NASH was observed, compared to normal liver histology in controls. Whereas controls showed only pericentral (zone 3) 4-HNE positivity, NASH livers demonstrated a panlobular positivity. After construction of liver lobules for analysis, DAB intensity and relative distance ranging from 0 (lobular edge) to 1 (centrolobular vein) displayed a gradient of 4-HNE with a steep decrease in positive area towards the portal triads in controls. However, NASH livers had a more widely distributed positivity shown as a plateau in all lobular zones. Comparing the periportal zone (defined as the periportal third of the defined liver lobule), the 4-HNE positive area was significantly higher in NASH compared to controls ($p=0.01$). Likewise, the method quantified panlobular GPX4 positivity in NASH compared to centrolobular positivity in controls, reaching significance comparing the periportal zone of NASH to controls ($p=0.01$). Importantly, upon exclusion of pixels pertaining to lipid vacuoles from analysis the percentage of 4-HNE and GPX4 positive area increased in all lobular zones in NASH, but not in controls. Hence, correcting for steatosis increased the difference in periportal 4-HNE and GPX4 positive area between NASH and controls ($p<0.01$ for both stains).
Conclusions: The method presented allows for accurate assessment and quantification of a differential positive pattern of IHC stainings across the liver lobule in both normal and severely steatotic livers. This method also allows correction for the confounding effect of non-staining lipid vacuoles that will normally result in an underestimation of the IHC positive area as empty vacuoles are not immunostained. Owing to its generic design this method may be applied in translational research to study the expression pattern of various epitopes in multiple diseases of the liver.

- A03 -

MONTH OF VIRAL HEPATITIS AT LOCAL PRIMARY CARE PRACTICES. M. Coessens (1), J. Schouten (2), W. Verlinden (2) / [1] Laboratory of Experimental Medicine and Pediatrics, University of Antwerp, Antwerp, Belgium, Gastroenterology and hepatology, [2] Vitaz, Sint-Niklaas, Belgium, Gastroenterology and hepatology.

Introduction: Viral hepatitis is still a major global health problem. In Belgium, a low-endemic country, a risk-based screening strategy for hepatitis B and C is in place. However, this strategy is not always well applied, causing patients to be missed. In addition, correct prevalence information is scarce. If we aim to achieve the WHO elimination targets and eradicate viral hepatitis by 2030, feasible screening guidelines need to be implemented now.

Aim: This study aims to assess the effect of a local screening project of HBV and HCV in two urban primary care practices (PCPs) and two urban community health centers (CHCs). This will contribute to the formulation of feasible HBV and HCV screening guidelines in Belgium.
Methods: This multicentric prevalence study was conducted in two urban 'standard' PCPs [Kemnet (9 general practitioners or GPs) and Vinka Huisartsen (4 GPs)] and two urban CHCs [WGC De Vlier (7 GPs) and GC Lokeren (6 GPs)] in the province of East-Flanders in Belgium. During "the month of viral hepatitis", informative posters and information brochures on HBV and HCV, were present in waiting rooms. Patients, from whom a blood test had to be taken in routine clinical practice, were invited to have their HBV and HCV status checked. Patients that were not in need of a blood test, but that wanted to know their HBV and HCV status after reading the brochures, were also included. Then, hepatitis B surface antigen (HBsAg) and HCV antibodies (HCV Ab) were determined. Patient inclusion took place from March to June 2022 and was performed by GPs and nursing staff. All adult patients that signed informed consent were eligible. The Wilson score, Taylor series, and Fisher exact test were calculated using OpenEpi software, version 3.
Results: In this prevalence study, serology results from 644 patients were analyzed. Of these, 387 results came from primary care practices (PCPs, 60.09%) and 257 came from community health centers (CHCs, 39.91%). In the CHCs, HBsAg seroprevalence was 2.72% (7/257), and this is higher than the HBsAg seroprevalence in the PCPs [0%, p=0.003, 95% CI (0.73;4.71)] and in the general Belgian population [(GBP) 0.7%, p=0.000 1]. A total of seven patients tested positive for HBsAg in CHCs, one of them was known to have a chronic hepatitis B infection and was already in follow-up. Of the remaining six patients, four patients were diagnosed in the past but were lost to follow-up. Two patients were newly diagnosed. In this way, six patients were (re-)introduced into care. The children of five study patients had already been vaccinated. In addition, three partners had already been vaccinated, one partner had a serology consistent with a past infection, and one partner was not aware of his HBV status. For two study patients, the HBV status of their relatives remained unknown. Seroprevalences of HCV Ab were 0.26% (1/387) in PCPs and this was not different from the seroprevalence found in CHCs [0%, p>0.99, 95% CI (-0.76;0.25)] or from the GBP (0.22%, p=0.87). Initially, three patients tested positive for HCV antibodies. However, HCV Ab positivity was confirmed in only one patient (two false positive test results), and she was already successfully treated for a chronic HCV infection. No new HCV infections were detected.
Conclusions: We found the HBsAg seroprevalence to be higher in urban community health centers than in urban primary care practices in Flanders. All patients that tested positive for HBsAg, were first-generation migrants (not born in Belgium). Another Belgian HBV prevalence study reported a higher HBsAg seroprevalence in first-generation migrants (FGM, 2.55%). In the future, we need to assess whether an HBV screening strategy targeting FGM as a high-risk group, is cost-effective in Belgium. A Flemish study compared the HCV Ab seroprevalence in an urban community health center (2.54%) and a non-urban primary care practice (0.89%). In contrast, we found a lower HCV Ab seroprevalence, despite a similar study design. However, our data are in accordance with data from Litzroth et al (2019), where HCV seropositivity was reported to be 0.22% in the general Belgian population.

- A04 -

OUTCOMES OF LIVER TRANSPLANTATION FOR HEPATOPULMONARY SYNDROME IN PATIENTS WITH CONCOMITANT RESPIRATORY DISEASE. Ö. Koc (1), D. Aslan (2), M. Kramer (3), J. Verbeek (2), H. Van Malenstein (2), S. Van der Merwe (4), D. Monbaliu (5), R. Vos (6), G. Verleden (7), J. Pirenne (5), F. Nevens (4) / [1] Hasselt University, Hasselt, Belgium, Gastroenterology and Hepatology, [2] University Hospitals Leuven, Belgium, Department of Gastroenterology and Hepatology, [3] Maastricht University Medical Center, The Netherlands, Department of Gastroenterology and Hepatology, [4] University Hospitals Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology, [5] University Hospitals Leuven, Leuven, Belgium, Department of Abdominal Transplant Surgery and Coordination, [6] University Hospitals Leuven, Leuven, Belgium, Department of Respiratory Diseases, [7] University Hospitals Leuven, Belgium, Department of Respiratory Diseases.

Introduction: Concomitant respiratory disease is a common finding in patients with hepatopulmonary syndrome (HPS).
Aim: Among patients who underwent liver transplantation (LT) for HPS, we compared characteristics and outcome of patients with vs. without concomitant respiratory disease.
Methods: This monocentric retrospective observational study included patients with HPS who underwent LT between 1999 and 2020.
Results: During the study period, 32 patients with HPS received a LT; 9 (28%) with concomitant respiratory disease of whom one required a combined lung-liver transplantation. Patients with concomitant respiratory disease had higher PaCO2 (38 vs. 33 mmHg, p = 0.031). The 30-day postoperative mortality was comparable, but the estimated cumulative probability of resolution of oxygen therapy after LT in HPS patients with vs. those without concomitant respiratory disease was lower: 63% vs. 91% at 12 months and 63% vs. 100% at 18 months (HR 95% CI 0.140–0.995, p=0.040). In addition to the presence of concomitant respiratory disease (p=0.040), history of smoking (p=0.012) and high baseline 99mTcMAA shunt fraction (>20%) (p=0.050) were significantly associated with persistent need of oxygen therapy. The 5-year estimated cumulative probability of mortality in patients with concomitant respiratory disease was worse: 50% vs. 23% (HR 95% CI 0.416–6.867, p=0.463).

Conclusions: The presence of a concomitant respiratory disease did not increase the short-term postoperative mortality after LT in patients with HPS. However, it resulted in a longer need for oxygen therapy and a worse 5-year survival.

- A05 -

SINGLE-CELL AND SINGLE-NUCLEUS SEQUENCING ON HUMAN TRANSJUGULAR LIVER BIOPSIES: PROOF OF CONCEPT AND WITHIN-PATIENT COMPARISON. L. Van Melkebeke (1), J. Verbeek (1), D. Bihary (2), H. Korf (1), D. Lambrechts (2), S. van der Merwe (1) / [1] KUL - University of Leuven, Leuven, Belgium, Laboratory of Hepatology, [2] VIB Center for Cancer Biology, Leuven, Belgium, Center for Cancer Biology.

Introduction: Transjugular liver biopsies (TJB) are the only safe way to collect liver tissue in patients with ascites and/or coagulation disorders. Both single-cell (sc-RNAseq) and single-nucleus RNA sequencing (sn-RNAseq) are powerful tools that allow transcriptomic profiling of thousands of individual cells. So far, no protocol is available for sc-RNAseq or sn-RNAseq on these small and fragile TJB's.
Aim: We aimed to validate a protocol of sc-RNAseq and sn-RNAseq in TJB's and compare both techniques within-patient.
Methods: A protocol was developed for sc-RNAseq and sn-RNAseq on TJB's. A within-patient comparison was made between both techniques in 3 patients. Raw sequencing reads were aligned to the human reference genome (GRCh38/hg38) and gene-expression matrices were generated with CellRanger (v3.0.2). For downstream analysis and statistical analysis R (v.4.1.2, with respective packages: e.g. Seurat, Doubletfinder, EnhancedVolcano, gprofiler2) and GraphPad Prism v9.0 were used. Normally distributed data are reported as mean ± standard deviation, non-normally distributed data are reported as median with interquartile range. Normality was tested using the Shapiro-Wilk test. Depending on the type of data, a paired sample t-test or Wilcoxon matched-pairs signed ranked test were used to compare cell numbers and percentages. Significance was defined as a two-sided test ($p < 0.05$).
Results: In total 31,055 single nuclei and 6,160 single cells were identified in TJB's of all 3 patients together, with a significantly higher number of nuclei than cells per patient sample (10,352±3,567 vs. 2,053±1193, $p<0.05$) and a significantly higher number of genes per nuclei than per cell (2,873±195 vs. 2,261±21, $p<0.05$). All major hepatic cell types could be identified in both sc-RNAseq and sn-RNAseq: hepatocytes, cholangiocytes, mesenchymal cells, endothelial cells, T-cells, B-cells and myeloid cells. Furthermore, these major cell types could be subclustered into 20 different known minor cell types. There was a significantly lower percentage of T-cells (2.14%±2.04 vs. 18.93%±4.29, $p<0.05$) and endothelial cell (11.78%±1.56 vs. 43.32%±5.67, $p<0.01$) in sn-RNAseq compared to sc-RNAseq, but a significantly higher percentage of hepatocytes (24.60%±6.56 vs. 1.61%±0.4, $p <0.05$). For the minor cell types, there was a significantly lower percentage of vascular smooth muscle cells (20.39%±6.41 vs. 68.30%±11.30, $p <0.05$), hepatic artery endothelial cells (7.43%±3.75 vs. 14.32%±5.52, $p <0.05$) and infiltrating monocytes (8.99%±2.27 vs. 43.29%±11.25, $p<0.05$) and a significantly higher percentage of liver sinusoidal endothelial cells (10.19%±3.03 vs. 1.56%±1.21, $p <0.05$) in sn-RNAseq compared to sc-RNAseq. In absolute numbers, there was a significantly higher number of hepatocytes in sn-RNAseq (2402±275 vs. 31±14, $p<0.01$) compared to sc-RNAseq. The majority of the top upregulated differentially expressed genes (DEGs) in each cell type obtained with one technique was also highly (LogFC > 0.75) and significantly (adjusted $p < 5x10-50$) upregulated in the other technique (67 out of 68 DEGs). Furthermore, the top upregulated functional pathways of different cell types were also highly comparable between both techniques.
Conclusions: A working protocol to use sc-RNAseq and sn-RNAseq was developed for TJB's, enabling the processing of liver tissue over the whole range of liver diseases. Furthermore, a direct comparison showed major significant differences in cell type composition between the two techniques. Importantly, the gene signatures and functional pathways of different cell types were highly comparable in both techniques. This information will help researchers to make an informed decision on the type of technique to be implemented based on the underlying research question and cell type of interest.

- A06 -

ALAGILLE SYNDROME LIVERS DISPLAY PREMATURE SENESCENCE. G. Jannone (1), C. de Magnée (2), R. Tambucci (2), J. Evraerts (1), J. Ravau (1), M. Najimi (1), E. Sokal (1) / [1] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, IREC-PEDI, [2] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Surgery.

Introduction: Alagille syndrome (ALGS) is an autosomal dominant disease characterized by a multisystem involvement including bile duct paucity and cholestasis and caused by JAG1 or NOTCH2 mutations in most of the cases. Jagged1-Notch2 interactions are known to be crucial for intrahepatic biliary tract development, but the Notch signalling pathway is also involved in the juxtacrine transmission of senescence and in the induction and modulation of the senescence-associated secretory phenotype (SASP).
Aim: Our aim was to investigate premature senescence in ALGS liver to better understand the involvement of Notch in senescence and SASP development.

Methods: Liver tissue from ALGS patients was prospectively obtained at the time of liver transplantation (n=5) and compared to control livers (n=5).
Results: We evidenced advanced premature senescence in the livers of five JAG1 mutated ALGS paediatric patients through increased senescence-associated beta-galactosidase activity ($p<0.05$), increased p16 and p21 gene expression ($p<0.01$), and increased p16 and γH2AX protein expression ($p<0.01$). Senescence was located in hepatocytes of the whole liver parenchyma as well as in remaining bile ducts. However, classical SASP markers (TGF-β1, IL-6, IL-8) were not overexpressed in the livers of our patients.
Conclusions: We demonstrate for the first time that ALGS livers display important premature senescence despite Jagged1 mutation, but we could not evidence any increase of SASP markers in our cohort, possibly due to a disrupted SASP induction caused by abnormal Notch signalling.

- A07 -

THE PREVALENCE OF NAFLD AND NAFLD-RELATED FIBROSIS IN PATIENTS WITH ACUTE CORONARY SYNDROME: PRELIMINARY RESULTS OF A PROSPECTIVE STUDY. W. Robaeys (1), L. Heyens (1), M. Dupont (2), K. Ameloot (2), G. Robaeys (1), M. Struyve (3), G. Stockmans (3), L. Bruckers (4), J. Penders (5), S. Francque (6) / [1] Hasselt University, Hasselt, Belgium, Faculty of health and life sciences, [2] Ziekenhuis Oost Limburg (ZOL), Genk, Belgium, Cardiology, [3] Ziekenhuis Oost Limburg (ZOL), Genk, Belgium, Gastroenterology and hepatology, [4] Hasselt University, Hasselt, Belgium, Centre for statistics, [5] Ziekenhuis Oost Limburg (ZOL), Genk, Belgium, Clinical biology, [6] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology and hepatology.

Introduction: The estimated prevalence of NAFLD in adults is between 20-30%. This might be increased in acute coronary syndrome (ACS). NAFLD has been described as an independent contributor to the pathology of ACS.
Aim: To study the prevalence and staging of NAFLD in patients with an ACS.
Methods: Between February and October 2022, adult patients with an ACS were prospectively recruited in a monocentric, in-hospital, cohort study (ZOL). Patients with a history of chronic liver disease, excessive alcohol use, or secondary causes of steatosis were excluded. A Fibroscan® measurement and non-invasive blood scores for steatosis (Fatty Liver Index (FLI), hepatic steatosis index (HSI)), fibrosis (FIB-4), and fibrotic NASH (FAST) were obtained in patients being fasting for minimally three hours.
Results: Sixty-six patients diagnosed with an ACS were included. The mean age was 64.3±8.7. Overall, 51 patients (77%) were male, 11 (17%) had arterial hypertension, 12 (18%) type 2 diabetes, 39 (59%) metabolic syndrome. The frequency of one, two, three-vessel disease was 25 (39%), 20 (31%), 20 (31%) while of STEMI, Non-STEMI, unstable angina 30 (46%), 33 (50%), 3 (4%), resp. Using the M-probe of Fibroscan®, 16 patients (24%) had fibrosis (LSM≥7.9kPa), 8 stage 4 fibrosis (LSM>10.3kPa); 51 patients (77%) steatosis (CAPTM≥215dB/m), 17 (26%) stage 1 steatosis (215-252dB/m), 16 (24%) stage 2 steatosis (252-296dB/m), and 18 (27%) stage 3 steatosis (≥296dB/m). Using FLI (n=57) and HSI (n=61), 24 (36%) and 59 (89%) patients had steatosis, respectively. FIB-4 (n=64) and FAST-score (n=58) were elevated in respectively 43 (65%) (>1.3) and 6 (9%) (>0.67) patients. Preliminary correlation analyses between NAFLD and CAD were not significant.
Conclusions: Preliminary results of this prospective, monocentric, cohort study demonstrate an increased prevalence of steatosis, but also, fibrosis in patients with ACS. Whilst further study is awaited, these data support screening for NAFLD in patients with ACS.

- A08 -

THE INSULIN SENSITIVITY INDEX DERIVED FROM EUGLYCEMIC CLAMPS IS CORRELATED TO LIVER FAT CONTENT DETERMINED BY MAGNETIC RESONANCE SPECTROSCOPY IN TYPE 1 DIABETES. J. Mertens (1), M. Braspenning (2), F. Vanhevel (3), M. Spinhoven (3), S. Francque (1), C. De Block (2) / [1] Antwerp University Hospital, Edegem, Belgium, Gastroenterology and Hepatology, [2] Antwerp University Hospital, Edegem, Belgium, Endocrinology, Diabetology and Metabolism, [3] Antwerp University Hospital, Edegem, Belgium, Radiology.

Introduction: Insulin resistance is proposed as a causative factor of non-alcoholic fatty liver disease (NAFLD) in the general population. Reports on NAFLD in type 1 diabetes (T1D) are increasing, but whether insulin resistance is linked to NAFLD in this population needs elucidation. Furthermore, people with T1D are an excellent model to investigate insulin resistance in relation to NAFLD without confounding by autologous insulin production.
Aim: We aimed to assess whether the index of insulin resistance is correlated with liver fat content (LFC) in adults with T1D without causes of secondary liver fat accumulation.
Methods: A 40 mU/m2 per minute hyperinsulinemic-euglycemic clamp (HEC) was performed according to DeFronzo et al. LFC was measured by magnetic resonance spectroscopy (MRS) and calculated as the mean of three independent regions of interest. NAFLD was diagnosed by mean LFC > 5.56 % and NAFLD subjects were matched 1:1 to no-NAFLD controls with T1D based on age and sex.

Results: Twenty subjects with a mean age of 48 ± 17 years, a BMI of 27.3 ± 4.3 kg/m2, and an HbA1c of 7.3 ± 0.8 % were included. The mean M-index (HEC-derived index of insulin sensitivity) was 5.12 ± 3.03 mg/kg/min. Mean LFC was 15.6 ± 8.3 % (NAFLD) versus 2.8 ± 1.4 % (controls), $p < 0.001$. The mean M-index differed significantly (2.88 ± 1.58 [NAFLD] vs. 6.74 ± 2.11 [controls] mg/kg/min, $p < 0.001$). BMI was significantly higher in the NAFLD group (29.6 ± 3.6 vs. 25.1 ± 3.8 kg/m2, $p = 0.014$). There was a strong correlation between the M-index and LFC ($r = -0.85$, $p < 0.001$) . Linear regression showed that the M-index (B = -1.504, 95% CI: (-2.9 to -0.101), $p = 0.037$) and BMI (B = 0.879, 95% CI: (0.047 to 1.711), $p = 0.040$) but not age nor HbA1c were associated with LFC.
Conclusions: HEC-derived measures of insulin resistance are strongly correlated to LFC in people with T1D, independently from BMI. These data support the pivotal role of insulin resistance in NAFLD pathophysiology and as a therapeutic target for the treatment of NAFLD.

- A09 -

SURVIVAL OF PLACEBO-TREATED PATIENTS WITH SEVERE ALCOHOLIC HEPATITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS. L. Van Melkebeke (1), L. Pollentier (2), S. van der Merwe (1), F. Nevens (1), J. Verbeek (1) / [1] KUL - University of Leuven, Leuven, Belgium, Laboratory of Hepatology, [2] KUL - University of Leuven, Leuven, Belgium, Faculty of medicine.

Introduction: Severe alcoholic hepatitis (sAH) is one of the most devastating presentations of alcohol-related liver disease, with a mortality rate of around 20-40% at 1 month. However, our therapeutic arsenal is limited. Corticosteroids may improve survival at 1 month, but not at 90-day or 1 year follow-up. Therefore, there is a high need for the development of effective drugs.
Aim: Via a systematic review and meta-analysis, we assessed the survival of placebo-treated sAH patients to estimate the natural course of the disease, which is crucial information for the design of therapeutic trials in these patients.
Methods: We performed a systematic search in Pubmed, Embase, Cochrane Library and Web of science for randomized controlled trials (RCT) in sAH comparing an active treatment to placebo published until 03/2021. Patient characteristics including survival of patients in the placebo group at 1 month and 90 days were collected. Data were analyzed on study-level using a linear mixed model as described by DerSimonian and Laird, with the arcsin-transformed survival rates as outcome. A two-sided p-value of < 0.05 was considered statistically significant.
Results: Eleven studies (total number of placebo-treated sAH patients = 568) were eligible for meta-analysis. Pooled 1-month survival was 72.93% (95% CI 67.09%-78.39%, 568 patients, 11 RCT's) and pooled 90-day survival was 73.61% (95% CI 68.18%-78.69%, 269 patients, 2 RCT's) in sAH patients treated with placebo. A more recent year of publication was positively associated with 1-month survival (regression coefficient (RC) 0.0053, 95%CI 0.0017-0.0089, p=0.0037, 11 RCT's). Notably, the last two European trials (n= 289), had a survival of >80%. Creatinine level was negatively associated with 1-month survival (RC -0.1407, 95%CI -0.2281 - -0.0534, p=0.0016). After correction for year of publication, creatinine level remained significantly associated with 1-month survival (RC -0.1042 (-0.1992 - -0.0091, p=0.0320).
Conclusions: One-month and 90 days survival of sAH patients treated with placebo is over 70%, with one-month survival being more than 80% in the most recent trial. These relatively favorable outcomes have major implications for the sample size calculation of new trials in sAH, questioning the feasibility of demonstrating superiority over placebo in classical RCT design.

- A10 -

ADVERSE OUTCOMES ARE FREQUENT AND NOT RELATED TO INITIAL HDV VIRAL LOAD IN HEPATITIS DELTA INFECTIONS IN BELGIUM. A. Furquim d'Almeida (1), E. Ho (2), L. Govaerts (2), T. Sersté (3), M. Peeters (4), P. Michielsen (2), S. Bourgeois (5), C. Moreno (6), H. Van Vlierberghe (7), C. de Galocsy (8), E. Padalko (9), S. Van Gucht (4), T. Vanwolleghem (2) / [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] CHU Saint-Pierre, Brussels, Belgium, Department of Hepatogastroenterology, [4] Sciensano, Brussels, Belgium, National Reference Centre of Hepatitis Viruses, [5] ZNA Antwerpen, Antwerpen, Belgium, Department of Gastroenterology, [6] CUB Hôpital Erasme, , Belgium, Department of Gastroenterology, [7] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology, [8] Hôpitaux Iris Sud Bracops, Brussels, Belgium, Department of Gastroenterology and Hepatology, [9] Ghent University Hospital, Ghent, Belgium, Laboratory of Medical Microbiology.

Introduction: Hepatitis delta virus (HDV) is a defective RNA virus that requires hepatitis B virus (HBV) for its replication. The prevalence and disease burden of HDV in Belgium is underestimated. Persistent HDV viremia has been shown to be associated with adverse outcomes. However, available in-house and commercial HDV RNA assays vary widely in sensitivity and genotype specificity. Until recently there was no approved therapy for HDV.

Aim: We examined the disease severity and outcomes of patients with hepatitis delta in Belgium. In addition, we aimed to investigate the differences in disease severity in multiple subpopulations of this cohort.
Methods: In the present study we retrospectively performed a medical chart review of hepatitis delta patients seen at 6 Belgian hospitals. All relevant data, including lab results, radiography findings, biopsies and consultation notes, were collected from July 2001 until October 2022. The inclusion criteria were a) HBsAg or HBV DNA positive at admission; b) anti-HDV or HDV RNA positive; c) available medical file with initial biological and clinical evaluations; d) at least 1 follow-up visit. Severe outcomes were defined as either a) liver decompensation, b) HCC diagnosis, c) liver transplantation or d) death.
Results: A total of 100 HDV positive patients were included. The median age was 35 years (range 6 – 61 years). Patients were predominantly male (57.9%) and had a median follow-up of 5.43 years (range 0.17 – 20.41 years). The median time until HDV diagnosis was 0.13 years (max 17.9 years). The median ALT and MELD score at admission were 77.5 U/L (range 13 – 5450 U/L) and 7.88 (range 6 – 37) respectively. For 86/100 patients a biopsy or non-invasive liver fibrosis assessment was available, showing cirrhosis in 37.2% of the patients (13 on biopsy and 19 with an elastography >= 12 kPa). Cirrhosis was diagnosed at a median age of 41 years (range 13 – 60 years). A HDV RNA assay was performed in 91/100 patients, of which 68 (74.7%) had a positive result. Different HDV RNA assays have been applied in our real-world cohort, both in-house (mostly before 2014) as commercially available (mostly after 2014). The mean ALT was significantly higher at admission in patients with a positive HDV RNA (136 U/L vs 63 U/L, $p<0.001$). There was no significant difference in age ($p = 0.48$), presence of cirrhosis ($p = 0.85$) and MELD score at admission ($p = 0.22$) between these groups. A total of 25 patients had at least one severe outcome: 19 liver decompensations (of which 5 at admission), 8 HCC's (1 at admission), 3 liver transplantations and 9 deaths. The 1-, 5- and 10-year cumulative outcome probability was 16%, 21% and 39% respectively. The median age at first outcome was 49 years (range 25 – 61 years). After accounting for age, there was no association between a positive HDV RNA result and having a severe outcome ($p = 0.82$). Importantly, repetitive HDV RNA assays were only available in 52% of the patients and in 36% of the patients with a severe outcome the HDV RNA assay was performed after the clinical outcome was observed. The fact that no association was found questions the prognostic value of a one-time HDV RNA assay and suggests that this may not be representative for the HDV activity during the whole follow-up.
Conclusions: HBV-HDV coinfections lead to severe liver-related outcomes in almost 40% of patients within 10 years in Belgium. The lack of an association between HDV RNA positivity performed by different assays and outcomes in our study, calls for standardization of HDV RNA assays. In addition, we advocate to periodically monitor the HDV viral load with newest assays in order to detect persistent viremia or late HDV RNA relapses after initial negative results.

- A11 -

MYOSTEATOSIS IN THE LIVER TRANSPLANT CANDIDATE: IS IT THE FUTURE PROGNOSTIC MARKER?
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Introduction: The body composition of the cirrhotic patient plays an important role in his prognosis. Several factors such as loss of skeletal muscle mass, malnutrition, and frailty (assessed by liver frailty index LFI) are closely associated with an increased risk of mortality in the liver transplant list. Myosteatosis is defined as the pathological excess of fat within the muscle expressed as a lower mean skeletal muscle radiodensity on computed tomography. Several studies have recently observed a negative impact of myosteatosis on the outcome of cirrhotic patients as well as in the postoperative outcome of patients undergoing liver transplantation (LT). There are still questions about the impact of this myosteatosis on liver function and on muscles functionality.
Aim: The aim of this study is to define the impact of skeletal muscle mass and composition on the morbidity and mortality on the waiting list for LT.
Methods: This single-center prospective observational study screened adult patients who were candidates for LT from June 2021 to September 2022. Each candidate received a complete nutritional and functional assessment during its pre-transplant evaluation. Low muscle mass (skeletal muscle mass index, SMI) and myosteatosis (muscle density attenuation) were measured on a cross-sectional area of the third lumbar vertebral level (L3) using a CT scanner and SliceOmatic

program. Low muscle mass was defined as SMI < 39 cm2/m2 in females and < 50cm2/m2 in males. Myosteatosis was assessed by skeletal muscle radiodensity attenuation (SM-RA) and the cut-off were SM-RA < 41 HU for patients with a BMI < 24.9 kg/m2 and < 33 HU for patients with a BMI 25 kg/m2. Frailty was calculated using the Liver Frailty Index (LFI). This score consists in evaluating grip strength, chair stands, and balance testing. Time-to-event analysis was performed using Kaplan-Meier method to investigate the impact of nutritional and function variables on outcome. One-year survival was determined after censoring for patients who underwent LT during this period. Univariate and multivariate Cox proportional hazard regressions were computed to identify predictors of morbidity and mortality on the waiting list for LT.

Results: 103 patients were screened during this period, of which 84 were placed on the Eurotransplant liver transplant waiting list. The mean age was 54 years and 67,7% were males. The primary etiology of liver disease was alcohol and 38% of patients were listed for hepatocellular carcinoma. 26.6% of patients had low muscle mass and 31% had myosteatosis. Most patients were pre-frail (54.4%) and 15.5% were frail based on LFI. The one-year patient survival probability on the waiting list was 76,9±7,2%. The patients presented a one-year risk of 33% for the development of a cirrhosis decompensation needing a hospitalization. In univariate analysis, the presence of myosteatosis was strongly associated with one-year mortality (HR 10.22 (2.16-48.29, p=0.003)). Patients with myosteatosis were frailer (LFI 3.96±0.72 vs 3.51±0.72 p= 0.014). Their grip test was also lower compared with patients without myosteatosis (26.3±8.08 vs 31.7±11.4 p=0.02) The survival probability was significantly reduced in patients with myosteatosis compared with patients with higher SM-RA values (43±17% vs 95±4%, p<0.001). However, this was not significant after adjustment for cirrhosis severity assessed by the MELD score (HR = 4,65 (0,93-23,2) p=0,06). The probability of urgent hospitalization for liver decompensation was also increased in the myosteatotic patients (59±18% vs 23±8%, p=0.012).

Conclusions: Among all muscle parameters and beside the MELD score, myosteatosis is a strong predictor of morbidity and mortality on the waiting list for LT. It is associated with lower functional capacity and higher frailty. A composite score including parameters of liver function on the one hand and myosteatosis on the other hand would probably make it possible to better discriminate and prioritize patients on the LT waiting list. Appropriate cut-offs for cirrhotic patients should also be determined.

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APPLICATION OF UPDATED DIAGNOSTIC CRITERIA FOR CIRRHOTIC CARDIOMYOPATHY: EVALUATION OF ITS CLINICAL IMPACT IN LIVER TRANSPLANTATION CANDIDATES. F. Voet (1), M. Khalenkow (1), E. Vander Straeten (1), M. De Pauw (2), H. Degroote (3), X. Verhelst (3), A. Geerts (3), H. Van Vlierberghe (3), S. Raevens (3) / [1] Ghent University, Ghent, Belgium, Student, [2] Ghent University, Ghent, Belgium, Cardiology, [3] Ghent University, Ghent, Belgium, Gastroenterology and hepatology.

Introduction: Cirrhotic cardiomyopathy (CCMP) is a liver-related cardiac complication that can occur in patients with cirrhosis. CCMP is characterized by the presence of diastolic dysfunction and/or systolic dysfunction (DD and SD). Diagnostic criteria were first established by the Montréal consensus in 2005, however, they substantially lacked specificity. With the application of tissue Doppler imaging, the evaluation of DD has significantly evolved, and diagnostic criteria have been revised since 2019. The prevalence and the clinical impact of CCMP in liver transplantation (LT) candidates are not well studied.

Aim: In this single-center retrospective study, we aimed to estimate the prevalence of CCMP, applying the 2019 criteria, in our population of LT candidates. We assessed the impact of DD and CCMP on waitlist mortality and post-LT outcome and explored if DD and CCMP can improve after LT.

Methods: Demographic, clinical, echocardiographic and outcome data of 522 adult patients on the waitlist for LT between 01/01/2005 and 31/03/2017 in the Ghent University Hospital were analyzed. CCMP, DD and SD were diagnosed based on the diagnostic criteria established in 2019, using tricuspid regurgitation velocity, e' lateral, and ejection fraction. Data were analyzed using SPSS.

Results: DD, SD and CCMP were diagnosed in respectively 5,7%, 1,5% and 8,1% of our patients evaluated for LT. This study further focused on DD and CCMP given the low prevalence of SD. Patients with DD and CCMP were significantly older compared to patients without DD or CCMP (mean age 65y versus 60y, and 63y versus 57y respectively, P<0.001). Other demographic data and clinical characteristics, e.g. etiology and severity of the underlying liver disease, were similar between LT candidates with and without CCMP/DD. The presence of DD did not significantly affect waitlist mortality: 8,9% without DD died on the waitlist versus 21,1% with DD. Patients who died on the waitlist were significantly older, had more severe liver disease, and more frequently had pulmonary comorbidities. A similar amount of LT candidates without DD underwent LT as LT candidates with DD (85.4% versus 73.6% respectively). The mean follow-up time in patients with and without DD was 1395 and 988 days (P=0,44) respectively. Post-LT survival was similar in both groups: 14,3% of patients with DD and 15,2% of patients without DD died during follow-up. Pulmonary comorbidities and higher e' lateral were more frequently seen in deceased patients. Follow-up echocardiographic data post-LT were available in 10 patients who were diagnosed with DD before LT: only 1 of them fulfilled the diagnostic criteria of DD post-LT.

Conclusions: This large cohort study indicates that the prevalence of CCMP among LT candidates is rather low (+/- 8%), and predominantly presents as DD. Our data suggest that the presence of DD does not significantly affect waitlist outcome or post-LT survival.

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IDENTIFYING THE ROLE OF GUT VASCULAR-ASSOCIATED MACROPHAGES IN LIVER CIRRHOSIS. L. Smets (1), M. Viola (2), H. Korf (1), F. Nevens (3), G. Boeckxstaens (2), S. van der Merwe (1) / [1] KUL - University of Leuven, Leuven, Belgium, CHROMETA - Laboratory of Hepatology, [2] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, CHROMETA - Laboratory for Intestinal Neuroimmune Interactions, [3] University Hospitals Leuven, , Belgium, Department of Gastroenterology and Hepatology.

Introduction: Liver cirrhosis is an end stage in the evolution of many types of chronic liver diseases. As cirrhosis worsens, there is a simultaneous breach in intestinal barrier integrity [1]. The disruption of this selective barrier, also referred to as 'the leaky gut' hypothesis, allows pathological bacterial translocation to the circulation which perpetuates systemic inflammation, bacterial infections and acute on chronic liver failure.
Aim: We hypothesize that a dysfunction of gut vascular-associated macrophages leads to a breach in the gut vascular barrier and consequently the translocation of bacteria to the systemic circulation and liver. Therefore, we investigated the changes in gut (vascular associated) macrophages in maintaining vascular integrity and their role in bacterial translocation during the development of experimental cirrhosis.
Methods: Liver cirrhosis was experimentally induced in mice by subcutaneous injection of CCl4 two or three times a week for up to 20 weeks. Picrosirius red staining of liver sections confirmed the appearance of fibrosis after 14 weeks, advanced fibrosis after 17 weeks and micro-nodular liver cirrhosis after 20 weeks of CCl4 exposure. For the depletion of gut vascular-associated macrophages, Cx3cr1CreERT2.Rosa26-iDTR (Cx3cr1-iDTR) mice were injected intra-peritoneally six times with diphtheria toxin (DTx) (with 48h intervals). To investigate the extent of bacterial translocation during liver disease progression, ileal loop experiments were performed, where we evaluated the amount of fluorescent signal in the liver after injecting fluorescent E.coli bioparticles into a closed-off ileal loop. The fluorescent signal was quantified by calculating the corrected total cell fluorescence (CTCF) value: CTCF = integrated density - (area of selected cell * mean fluorescence of background readings). To investigate the interconnectivity of macrophages lining the vasculature network, we stained peeled lamina propria of fibrotic and cirrhotic mice with an endothelial marker (VE-cadherin) and with a pan-macrophage marker (Iba1).
Results: Evaluation of the liver slices on immunohistological level following termination of the ileal loop experiment showed increased fluorescent signal of E. coli bioparticles in the livers during the fibrosis stage (14 weeks), reaching maximum levels at end-stage cirrhosis (20 weeks). Quantification of the fluorescent signal confirmed this observation, showing a significant increase in CTCF values at 17 and 20 weeks between cirrhotic and control animals. Notably, the amount of translocated bacterial particles in the livers of control animals was negligible. We next performed immunohistochemistry on the lamina propria obtained from CCL4 exposed animals to interrogate whether the macrophages lining the vasculature network closely interconnect with each other and moreover, tightly associate with vascular endothelial cells. The data revealed a disruption of the submucosal lamina propria macrophages interconnectivity with each other and with the vascular network, with progressive loss of Iba1+ macrophages during cirrhosis development (week 17 and 20). During the earlier fibrotic disease stage (week 14) the macrophages tightly lined the vascular network similar to what can be observed in the control condition. We next investigated whether the observed decrease in macrophages lining the gut vascular wall may be responsible for pathological bacterial translocation in liver cirrhosis. Hereto we quantified the amount of bacterial particles translocating to the liver following ileal loop experiments in in the Cx3cr1-iDTR mouse model whereby gut vascular intestinal macrophage have been depleted. The results indicated a significant accumulation of bacterial particles in the livers of vascular-associated macrophage-depleted mice. This data suggests that depletion of macrophages lining the vascular wall, leads to disruption of submucosal vascular barrier integrity and consequent increased bacterial translocation from the intestinal lumen to systemic sites.
Conclusions: Our findings demonstrate that in an experimental model of liver cirrhosis, bacterial translocation increases in parallel with progressive liver cirrhosis development. Furthermore, we demonstrate that a breakdown in the interconnectivity of intestinal lamina propria macrophages in lining the vascular network and a depletion of these macrophages coincides with increased bacterial translocation. These data suggest that macrophages around the blood vessels in the lamina propria are important in maintaining the vascular integrity. Ongoing research focuses on a possible causal link between the disruption of the vascular-associated macrophage network and the breach of gut vascular barrier integrity. References [1] Albillos A, et al. J Hepatol 2020.

- A14 -

ENHANCING MICROBIAL TRANSFORMATION OF BILE ACIDS TO PROTECT FROM NASH. J. Gillard (1), M. Roumain (2), C. Picalausa (1), M. Thibaut (3), G. Muccioli (2), A. Tailleux (4), B. Staels (4), L. Bindels (3), I. Leclercq (1) / [1] Université catholique de Louvain (UCLouvain), , Belgium, Laboratory of Hepato-Gastroenterology (GAEN),

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Introduction: While NAFLD represents the most common chronic liver disease worldwide, the mechanisms of disease progression, from simple steatosis to NASH, remain only partly described and there is no effective, safe and approved pharmacological treatment. Bile acids finely regulate immuno-metabolic pathways impaired in NAFLD by binding and activating bile acid-receptors such as FXR and TGR5. Hence, bile acids are attractive candidates for therapeutic development. An imbalance between primary bile acids – reflecting hepatic synthesis – and secondary bile acids – reflecting transformation by gut microbes – is a recurrent feature in humans and experimental models of NASH. We previously reported that secondary bile acids were low in mice with NASH (13% of the portal bile acid pool vs 36% in controls).
Aim: Here, we thus aimed at restoring the balance between primary and secondary bile acids by (1) a dietary supplementation with deoxycholic acid (DCA), a secondary bile acid, or (2) a probiotic approach to enhance the endogenous production of secondary bile acids by the gut microbiota. We evaluated the effects of both approaches on the composition and signaling of bile acids and on NASH progression.
Methods: We used foz/foz mice fed a high fat diet (HFD) as a model of NASH whose bile acid pool is depleted in secondary bile acids. For the dietary supplementation, foz/foz mice received a HFD containing DCA (0.1%) or a plain HFD for 12 weeks. For the probiotic treatment, at the introduction of the HFD, foz/foz mice received by oral gavage a fresh suspension of Clostridium scindens (10^9 CFU), a gut bacterial strain supporting the transformation of primary bile acids into secondary bile acids, or vehicle 3 times a week for 12 weeks.
Results: The supplementation of the HFD with DCA increased total bile acids, total secondary bile acids (45% of the portal bile acid pool) and DCA concentrations in foz/foz mice, shifting the bile acid pool towards a more TGR5- and FXR-agonistic pool. Notably, DCA elevated the TGR5 activation capacity of the portal blood (1.7- and 4.3-fold higher than WT controls and then untreated foz/foz mice, respectively). The restoration of bile acid signaling through DCA supplementation significantly lowered body weight gain, fasting glycemia and insulinemia and protected from NASH. Indeed, DCA reduced steatosis, macrophage infiltration and ballooning. Hence, only 15% of the treated mice still presented NASH, while 100% of the untreated mice met the criteria for NASH diagnosis. We next aimed at increasing endogenous DCA production by targeting the gut microbiota through a probiotic approach. We confirmed through a functional assay that Clostridium scindens has a 7α-dehydroxylase activity (i.e. it transforms primary bile acids into secondary bile acids). However, the administration of Clostridium scindens to foz/foz mice did not modulate the endogenous production of secondary bile acids, the portal bile acid pool and the activation of bile acid-receptors FXR and TGR5. Coherently, it had no effect on liver and metabolic phenotype, despite a massive increase of the faecal load of Clostridium scindens and its survival in the gut of treated mice.
Conclusions: The administration of Clostridium scindens did not enhance the endogenous production of secondary bile acids. A too low dose and frequency of administration, a too low biological effect of Clostridium scindens on a complex microbial community and/or a high bile acid 7α-rehydroxylation are possible explanations for the lack of impact of Clostridium scindens on the bile acid pool of a mouse model with a complex gut microbiota. Nevertheless, we demonstrated that the restoration of the balance between primary and secondary bile acids through a dietary supplementation with the secondary bile acid DCA protected from NASH and associated features.

- A15 -

ACUTE SPLANCHNIC VEIN THROMBOSIS IN PATIENTS WITH COVID-19. P. Deltenre (1), A. Payencé (2), L. Elkrief (3), V. La Mura (4), F. Artru (5), A. Baiges (6), L. China (7), I. Colle (8), E. Lemaitre (9), A. Marot (10), B. Procopet (11), D. Schiller (12), P. Rautou (2), A. Plessier (2) / [1] Clinique Saint-Luc, Bouge, Namur, Belgium, Division of Gastroenterology and Hepatology, [2] Hopital Beaujon, France, Hepatology, [3] CHU de Tours, France, Hepatology, [4] Ospedale Maggiore Policlinico, Milan, Italy, Hepatology, [5] CHUV Lausanne, Lausanne, Switzerland, Hepatology, [6] Hospital Clinic, Barcelona, Spain, Hepatology, [7] Royal Free Hospital, United Kingdom, Hepatology, [8] ASZ, Aalst, Belgium, Hepatology, [9] CHRU Lille, France, Hepatology, [10] CHU UCL Namur, Yvoir, Belgium, Hepatology, [11] Regional Institute of Gastroenterology and Hepatology, Romania, Hepatology, [12] Ordensklinikum Linz Barmherzige Schwestern, Austria, Hepatology.

Introduction: The natural history of splanchnic vein thrombosis (SVT) occurring during COVID-19 is unknown.
Aim: To assess the prognosis COVID-19 patients presenting with acute SVT and to assess if their disease profile differs from patients with acute SVT without COVID-19.
Methods: Retrospective study collecting health-related data of 23 patients with COVID-19 and acute SVT seen in 11 hospital centers belonging to VALDIG network and comparison to 494 patients with acute SVT included in a prospective database before the COVID-19 pandemic.

Results: Among the 23 COVID-19 patients presenting acute SVT, 20 had PVT with or without thrombosis of another splanchnic vein, 1 had superior mesenteric vein thrombosis, 1 had splenic vein thrombosis and 1 had hepatic vein thrombosis. No difference was observed in terms of age, sex ratio, liver tests, prevalence of an underlying prothrombotic condition and extension of SVT between patients with acute SVT and COVID-19 and those with acute SVT without COVID-19. Anticoagulation therapy was started in all COVID-19 patients on the day SVT was identified. During a median follow-up of 253 days (95% CI: 120-448 days), no patient suffered from gastro-intestinal bleeding or from another liver-related event. A single patient required intestinal resection. No patient died. At the end of the follow-up period, partial or complete recanalization of the splanchnic vein thromboses was observed in 38% of COVID-19 patients.
Conclusions: Patients presenting with SVT during COVID-19 have similar disease profile than non-COVID-19 patients with SVT. In this cohort study in which all patients received anticoagulation therapy, 6-month prognosis is excellent and partial or complete recanalization is observed in 38% of patients.

- A16 -

GLIAL TRANSCRIPTOMICS HIGHLIGHT EARLY INVOLVEMENT OF MICROGLIA AND INFILTRATING IMMUNE CELLS IN EXPERIMENTAL HEPATIC ENCEPHALOPATHY. W. Claeys (1), L. Van Hoecke (2), H. Lernout (3), C. De Nolf (2), E. Van Wonterghem (2), G. Van Imschoot (2), D. Verhaege (2), A. Geerts (4), C. Van Steenkiste (5), R. Vandenbroucke (2) / [1] Ghent University, Ghent, Belgium, Hepatology Research Unit, Liver Research Center Gent, [2] VIB Center for Inflammation Research, Gent, Belgium, Barriers in inflammation, [3] VIB Center for Inflammation Research, Gent, Belgium, Intestinal barrier signaling in disease and therapy, [4] Ghent University, Ghent, Belgium, Hepatology research unit, Liver research Center Ghent, [5] University of Antwerp, Antwerp, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Hepatic Encephalopathy (HE) is a frequent complication of liver cirrhosis, associated with poor outcomes, in which the interplay between ammonia and inflammation drives disease development. Astrocytes are the primary ammonia-metabolizing cell-type in the brain, while microglia are the main immunomodulatory brain cells. Astrocytes and microglia operate in concert in many acute and chronic neurological diseases, but in HE, understanding of glial cell function and interplay is lacking. We have previously established the bile duct ligation (BDL) mouse model as an experimental HE model (1) and shown that morphological changes in microglia precede those in astrocytes in this model.
Aim: This study aims to characterize the time-dependent changes in gene expression profiles as well as the functional consequences underpinning glial morphological changes in the BDL model of HE.
Methods: 10-12 week old male C57Bl/6j mice (n=6/group/timepoint) underwent BDL/sham surgery and were sacrificed 14 and 28 days after induction. Microglia (CD45intCD11b+) and astrocytes (CD45-CD11b-O1-ACSA2+) were isolated using FACS and RNA of isolated samples was sequenced. Gene set enrichment analysis (GSEA) and ingenuity pathway (IPA) upstream regulator analysis was performed. Results were validated in a separate cohort (n=6/group/timepoint) using qPCR. Transcriptomic profiles of astrocytes and microglia in the BDL model were compared to published gene expression profiles in other acute and chronic neurological diseases. Influx of immune cells was assessed through flow cytometry of whole brain single cell suspensions (n=6-8/group).
Results: BDL induces an early and sustained transcriptomic response in microglia, with differential expression (adjusted $p<0.05$, $|Log2FC|>1$) of 350 genes (290 up, 60 down) 14 days after induction and 448 (355 up, 93 down) 28 days after induction, with large overlap (226 genes) between both timepoints. At both timepoints, inflammatory signaling and chemotaxis pathways were significantly enriched. Immune phenotyping showed a time-dependent influx of Ly6Chi monocytes (x3,56 at 14d $p=0.0002$; x5,45 at 28d $p<0.0001$) and Ly6Ghi neutrophils (x2.83 at 14d $p=0.0091$; x4.22 at 28d $p<0.0001$) into the brain of BDL mice versus sham controls, while no changes were seen in T- or B-cells. TNF signaling was identified as the top regulator of microglial transcription at both timepoints, along with other cytokines (IL1b, IL6). GSEA revealed significant overlap of the microglial transcriptome in BDL mice at both timepoints with acute LPS-induced changes (14d $p=0.001$, 28d $p=0.002$) and disease-associated microglia found in Alzheimer's disease (14 days $p=0.001$, 28 days $p=0.02$) (2,3). In astrocytes, transcriptomic response was progressive, with 171 genes (108 up, 64 down) differentially expressed after 14 days, increasing to 495 (364 up, 131 down) 28 days after induction. 385 DEGs were unique to the 28d timepoint. Pathway enrichment was limited at 14 days, while inflammatory signaling pathways were significantly enriched 28 days after BDL surgery. Comparative analysis with published transcriptomic responses showed significant overlap with both LPS-induced A1 ($p<0.001$ at both timepoints) and ischemia-induced A2 ($p<0.001$ at both timepoints) astrocyte subtypes (4). GM-CSF was the top upstream regulator at both timepoints, while interferon related signaling (IFNbeta, IFNgamma, IRF7) and cytokines (IL1b, IL6) were uniquely found at the 28 day timepoint.
Conclusions: In experimental HE, microglia exhibit early and sustained transcriptomic changes pointing towards increased inflammatory signaling and immune cell attraction. Monocytes and neutrophils progressively accumulate in the BDL mouse brain, suggesting microglia drive this accumulation. While evidence of astrocyte reactivity can be found early after BDL, our data suggest a gradual response, with increased inflammatory signaling only later in the model. In both cell types, gene expression profiles are largely driven by cytokines, suggesting an important role for (peripheral) inflammation. This data provides useful insights to unravel the sequence of cellular changes in HE and direct future research into the interplay in the neuroimmune compartment in this disease. References 1. Claeys W, et al. Sci Rep. 2022

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18FDG PET SCANNER AS A SELECTION CRITERION IN LIVER TRANSPLANTATION FOR HEPATO-CARCINOMA. C. Lambrecht (1), M. Vandermeulen (1), M. Delbouille (1), J. Monard (1), A. Warmoes (1), C. Amicone (2), O. Warling (2), A. Lamproye (2), J. Delwaide (2), N. Meurisse (1), P. Honore (1), R. Hustinx (3), P. Lovinfosse (3), O. Detry (4) / [1] CHU of Liège, , Belgium, Abdominal Surgery and Transplantation, [2] CHU of Liège, , Belgium, Hepatogastroenterology, [3] CHU of Liège, , Belgium, Nuclear Medicine, [4] Centre Hospitalier Universitaire de Liège, Liège, Belgium, Abdominal Surgery and Transplantation.

Introduction: For years, Milan criteria have been the standard for selection criteria for liver transplantation (LT) of patients with hepatocellular carcinoma (HCC). Previous retrospective studies suggested that 18 FDG positron tomography (18FDG-PET) could be an effective tool to select HCC patients beyond Milan criteria for LT if their tumour is not FDG avid. A prospective national study evaluating the potential role of 18FDG-PET in LT for HCC was initiated by BeLIAC and financed by the National Cancer Foundation for the years 2019-2022. Complete results of this study with 2-year follow-up will be available by the end of 2024.
Aim: In this report the authors aimed to present the preliminary results of this study in the CHU Liege LT centre.
Methods: This study is a prospective national study accepted by all Belgian transplant centres and BeLIAC. All patients signed an informed consent form. Between January 2019 and October 2022, 51 patients (43 males, mean age 63y) were transplanted with HCC, and 44 had PET CT before LT or neoadjuvant therapy. Amongst these 44 HCC patients with PET, 28 were Milan-in, 1 Milan-in after successful downstaging, and 13 were Milan-out (11 Milan-out Up-to-seven-in and 2 Milan-out up-to-seven-out) at time of listing. Two Milan-in patients were PET positive, and all others were PET negative.
Results: Three patients died during the follow-up, without recurrence. No patients developed recurrence at 1- and 2-year follow-up. Three patients developed recurrence between 2- and 3-year follow-up and all were Milan-in. Importantly, no Milan-out PET negative patients developed recurrence at October 2022 follow-up.
Conclusions: Conclusions: PET FDG could be an important tool to offer potential LT opportunity to HCC patients outside Milan criteria. A longer follow-up and complete Belgian data are important before drawing further conclusions on this important matter.

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HEPATIC STELLATE CELL SINGLE CELL ATLAS REVEALS A HIGHLY SIMILAR ACTIVATION PROCESS ACROSS LIVER DISEASE AETIOLOGIES. V. Merens (1), S. Verhulst (1), L. van Grunsven (1) / [1] Vrije Universiteit Brussel (VUB), Jette, Belgium, Basic (Bio)Medical Sciences.

Introduction: Chronic liver disease (CLD) is a major cause of morbidity and mortality worldwide. The progression of CLD is characterized by excessive extracellular matrix deposition, thereby disrupting hepatic architecture and function. Hepatic stellate cells (HSCs) are the major source of this excessive collagen deposition in all underlying aetiologies of CLD. Upon liver injury, HSCs lose their ability to store vitamin A, differentiate towards a myofibroblast phenotype and become migratory, inflammatory, proliferative and fibrogenic. Several animal models such as common bile duct ligation, CCl4 intoxication and Western diets are used to model the different aetiologies of CLD, but to date, a comprehensive comparison between the mechanisms of activation of HSCs in different aetiologies has not been made.
Aim: In this study, we aimed to identify transcription factors responsible for the differentiation of HSCs towards myofibroblasts and to determine whether the transcriptional program differs between mouse liver injury models and human liver disease.
Methods: Mesenchymal cells, based on Pdgfrb expression, were selected from 7 single-cell RNA-Sequencing datasets describing 10 distinct mouse liver injuries. HSCs were selected from the merged mesenchymal atlas based on Lrat and Reln expression and were subjected to batch-effect removal, multidimensional reduction (UMAP) and Louvain clustering. The same approach was used to construct a human HSC atlas from 3 single-cell RNA-Sequencing datasets describing both healthy and cirrhotic livers. Transcription factor (TF) activity was calculated using pySCENIC. Pseudotime was calculated by trajectory inference using Slingshot on the TF activity matrix.
Results: First, a liver mesenchymal cell atlas was constructed to facilitate the identification of HSCs in all studies. HSCs could be clearly divided into 3 categories: Quiescent HSCs, which show a high expression of Lrat, Reln and Rgs5, Initiatory HSCs representing the first events of HSC activation characterized by high expression of YAP downstream targets Ankrd1 and Thbs1 and chemoattractant cytokines Ccl2 and Ccl7, while fully activated myofibroblasts show a high expression of collagens 1a1, 1a2, 3a1, 5a2 as well as classic HSC activation markers Loxl1 and Mmp2. HSCs isolated from mice without liver injury were primarily identified as quiescent HSCs, while HSCs isolated after acute and chronic liver injury were predominantly identified as initiatory HSCs and myofibroblasts respectively. Surprisingly, there are proportionally more quiescent HSCs after chronic liver injury than after acute liver injury, suggesting that HSCs

inactivate or are being replenished during chronic liver injuries. The transition from quiescent HSCs to initiatory HSCs and to myofibroblasts was validated by the sequential enrichment of their genesets in a time-resolved bulk RNA-Seq dataset of acute and chronic liver injury. Quiescent HSCs show high activity of several TFs known to be associated with quiescent HSCs like Ets2, Nr1h4 and Rxra. Upon injury, TFs of the activator protein 1-, NFκB- and EGR family become highly active, as well as Myc. In the fully activated myofibroblast population, Wt1, Prrx1, and Mef2c were highly active and predicted to be responsible for the regulation of HSC activation genes Col1a1, Col1a2 and Lox. To compare TF activity patterns of HSCs between injuries, trajectory inference was used to assign a pseudotime value to each cell as a proxy for their activation status. Comparison of the TF activity patterns revealed that there are no significant differences in TF activity patterns between the 7 different liver injury models. The distinction between quiescent- , initiatory- and fully activated HSCs in mouse liver injuries was validated in a human HSC activation atlas of healthy, fatty and cirrhotic livers. TFs identified to drive HSC activation in the mouse liver injury models also demonstrated similar activity patterns during HSC activation in humans.
Conclusions: We demonstrate that the transcription factors responsible for the activation of HSCs are conserved between mice and human and in all liver injury models studied. Our results strongly suggest that the testing or development of therapeutics preventing (further) activation of HSCs can be done in only one liver injury model. Additionally, we reveal novel TFs associated with activation of HSCs that are conserved in all liver injury models which could be used as novel targets for anti-fibrotic therapies.

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A MACHINE LEARNING-BASED CLASSIFICATION OF ADULT-ONSET DIABETES IDENTIFIES PATIENTS AT RISK FOR LIVER-RELATED COMPLICATIONS C. Zhan (1), L. Otero Sanchez (2), C. Gomes da Silveira (3), L. Crenier (3), H. Njimi (4), G. Englebert (1), A. Putignano (1), A. Lepida (1), D. Degré (1), N. Boon (1), T. Gustot (1), P. Deltenre (1), A. Marot (5), J. Devière (1), C. Moreno (1), M. Cnop (3), E. Trépo (1) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, [2] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology, [3] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Endocrinology, [4] Université Libre de Bruxelles, Belgium, Biomedical Statistics, [5] Clinique Saint-Luc Bouge, Namur, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Diabetes mellitus is a major risk factor for fatty liver disease development and progression. A novel machine learning method identified five clusters of patients with diabetes, with different characteristics and risk of diabetic complications using six clinical and biological variables.
Aim: We evaluated whether this new classification could identify individuals with an increased risk of liver-related complications.
Methods: We used a prospective cohort of patients with a diagnosis of type 1 or type 2 diabetes without evidence of advanced fibrosis at baseline recruited between 2000 and 2020. We assessed the risk of each diabetic cluster of developing liver-related complications, using competing risk analyses.
Results: We included 1068 patients, of whom 162 (15.2%) were determined to be in the severe autoimmune diabetes (SAID) subgroup, 266 (24.9%) were severe insulin-deficient diabetes (SIDD), 95 (8.9%) were severe insulin-resistant diabetes (SIRD), 359 (33.6%) were mild obesity-related diabetes (MOD), and 186 (17.4%) were in the mild age-related diabetes (MARD) subgroup. In multivariable analysis, patients in the SIRD cluster and those with excessive alcohol consumption at baseline had the highest risk for liver-related events. The SIRD cluster, excessive alcohol consumption, and hypertension were independently associated with clinically significant fibrosis. Using a simplified classification, patients assigned to severe and mild insulin-resistant groups had a 3- and 2-fold greater risk, respectively, of developing significant fibrosis compared to the insulin-deficient group.
Conclusions: A novel clustering classification adequately stratifies the risk of liver-related events and liver fibrosis in a diabetes population. Our results also underline the impact of the severity of insulin resistance and alcohol consumption as key prognostic risk factors for liver-related complications.

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BENEFITS OF SYSTEMATIC USE OF NON-INVASIVE FIBROSIS SCORES RATHER THAN FATTY LIVER INDEX IN TYPE 2 DIABETES PATIENTS: A PROSPECTIVE STUDY. Q. Binet (1), A. Loumaye (2), M. Hermans (2), N. Lanthier (1) / [1] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Service d'Hépato-Gastro-entérologie, [2] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Service d'Endocrinologie et Nutrition.

Introduction: Metabolic dysfunction-associated fatty liver disease (MAFLD) relates to steatosis occurring in the setting of a metabolic risk condition such as type 2 diabetes mellitus (T2DM). T2DM is an important risk factor for MAFLD

and vice-versa. Despite the high prevalence and serious clinical implications of MAFLD in patients with T2DM, it is often overlooked in clinical practice.
Aim: To assess the feasibility of outpatient systematic screening for MAFLD in T2DM patients. To do so, we determined the respective prevalence of steatosis and severe fibrosis using simple non-invasive tools, as per national guidelines (Francque S. Acta Gastroenterol Belg. 2018). We estimated patients' adherence to more accurate fibrosis screening by vibration-controlled transient elastography (VCTE) if indicated by clinical-biological testing.
Methods: We conducted a 12-month monocentric prospective study involving ambulatory T2DM patients who attended on a regular basis the diabetes clinic at Cliniques universitaires Saint-Luc between June 2021 and May 2022. Based on national and international guidelines, in case of positive screening for liver steatosis – using fatty liver index (FLI) – or advanced fibrosis – using a combination of non-alcoholic fatty liver disease fibrosis score (NFS) and fibrosis-4 (FIB-4) –patients were invited to undergo abdominal Doppler-ultrasound and/or VCTE. In case of elevated transaminase level, patients were further assessed to at least exclude viral hepatitis B and C, alpha-1-antitrypsin deficiency and biological markers of autoimmune hepatitis (elevated immunoglobulin G).
Results: A total of 213 patients were included in the study. 67.1 % of patients were male, mean age was 62 years and mean body mass index 31.3 kg/m². Three patients reported an alcohol consumption of more than 30 (male) or 20 (female) g/day. FLI classified most of the patients in the high (76.7 %) or indeterminate (18.8 %) risk category for steatosis, while only 4.5 % were classified as low risk. When contrasted with abdominal Doppler-ultrasound, the hepato-renal echogenicity gradient was increased in 80.5 % of patients with high or indeterminate risk based on FLI (>30). Twenty-two patients had dysmorphic liver and/or signs of portal hypertension. None of the patients presented with liver lesion compatible with hepatocellular carcinoma. The prevalence of advanced fibrosis varied greatly according to the different scores, ranging from 3.8 % (FIB-4) to 19.0 % (NFS). Whereas NFS seemed to classify the majority of T2DM patients (59.0 %) in the intermediate group, FIB-4 with age adjusted cut-offs classified most of the patients (75.1 %) in the low-risk group. Applying the guidelines and using a sequential combination of FLI and NFS/FIB-4, 29 (13.6 %) patients were proposed to undergo VCTE, with an acceptance rate of 89.3 %. As a result, 8 patients were diagnosed with cirrhosis (ie F4 and dysmorphic liver or signs of portal hypertension) and 15 patients were classified as advanced fibrosis (F3 or F4 without other evidence for cirrhosis at ultrasound). Of the 23 patients with VCTE-confirmed advanced fibrosis (F3-F4), 12 (52.2 %) had not previously been evaluated by an hepatologist, and therefore had newly diagnosed MAFLD of advanced stage. Sixty-one (28.6 %) patients had elevated transaminase levels. Besides 2 patients whose excessive alcohol consumption might underlie elevated liver tests, none of the patients had liver condition other than MAFLD.
Conclusions: Using simple clinicobiological non-invasive tools to routinely triage T2DM patients with potentially severe liver disease is feasible. There is a wide adherence of patients to non-invasive complementary exams such as abdominal Doppler-ultrasound and VCTE. The usefulness of FLI for steatosis detection in T2DM is questionable, as the vast majority of patients were classified as high or indeterminate risk for steatosis, meaning that nearly all T2DM presented with MAFLD. A baseline abdominal Doppler-ultrasound seems therefore appropriate in all T2DM patients, to assess liver surface, parenchyma and vascularization. The combined use of NFS and FIB-4, although presenting multiple shortcomings, allowed for detecting previously undiagnosed cirrhosis in 3.8 % and advanced fibrosis without cirrhosis in 7.0 %.

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FULLY CONTROLLED IPSC-DERIVED SPHEROIDS TO MODEL LIVER FIBROSIS. M. Kazemzadeh Dastjerd* (1), L. Cools* (1), A. Smout (1), V. Merens (1), H. Reynaert (1), N. Messaoudi (2), M. Kumar (3), C. Verfaillie (3), S. Verhulst (1), L. van Grunsven (1) / [1] Vrije Universiteit Brussel (VUB), Jette, Belgium, Liver Cell Biology research group (LIVR), [2] Vrije Universiteit Brussel (VUB), Jette, Belgium, Department of Surgery, UZ Brussel, [3] KU Leuven - University of Leuven, Leuven, Belgium, Stem Cell Institute Leuven.

Introduction: Chronic liver injury leads to overproduction of scar tissue, known as fibrosis. If left untreated, long-term injury can eventually result in the development of liver cirrhosis, which leads to 1 million deaths per year worldwide. During liver injury, damaged hepatocytes activate the hepatic stellate cells (HSCs), which play a pivotal role in the wound healing response by depositing excessive amounts of extracellular matrix. If the injury persists, this ultimately results in the development of liver fibrosis. Unfortunately, there are currently no FDA-approved anti-fibrotic drugs available. This is partially due to the lack of adequate human in vitro models that recapitulate the cellular composition and function of the human liver.
Aim: The goal of this study was to develop a human spheroid model to mimic liver fibrosis by using induced pluripotent stem cell (iPSC)-derived hepatoblasts (iHepatoblasts), hepatic stellate cells (iHSCs), endothelial cells (iECs) and macrophages (iMφ).
Methods: iPSCs (Sigma IPSC0028-1VL) were independently differentiated into iHepatoblasts, iHSCs, iECs and iMφ (Kumar et al., Biomaterials, 2021), before assembly into free floating spheroids by culturing cells in 96-well U-bottom plates and orbital shaking for up to 21 days. Differential expression and Gene Ontology (GO) analysis were carried out within R on bulk RNAseq samples. Functionality of iHSCs was tested by activation with TGF-β (48h) or through iHepatocyte (iHep) damage with acetaminophen (APAP) (72h) until day 13. Primary human liver spheroids were

generated using liver resections obtained from UZ Brussel from which hepatocytes were freshly isolated with a Percoll gradient and HSCs (UV+), ECs (CD32+) and Kupffer cells (CD45+ CD163+) by FACS.
Results: Since we incorporate iHepatoblasts in spheroids that need to mature to iHeps and since HSCs play a crucial role in chronic liver diseases, we used iHep maturation and iHSC activation as readouts for the optimisation of cell ratios in the spheroids. This resulted in an optimised ratio of 2 iHSC : 1 iHepatoblast : 0.6 iEC : 0.6 iMφ. We compared differentiation towards mature iHeps in 3D co-cultures to differentiation in 2D iHep monocultures (21 days). We detected higher gene expression levels of mature hepatocyte markers at day 21 of spheroid cultures compared to 2D cultures. This suggests that differentiating iHeps in 3D in the presence of other liver cell types is beneficial for their maturation. To evaluate the liver cell types in co-culture spheroids further, we performed RNAseq at the start (day 1) and at the end (day 21) of spheroid cultures. GO analysis showed that day 1 cells were still actively in the cell cycle, while spheroids cultured for 21 days showed high expression of genes involved in metabolic processes, i.e. phase I and II metabolism, drug and bile acid metabolism and gluconeogenesis. Similar to Hep markers, EC (PECAM1) and Mφ (ITGAM) markers increased over time, suggesting further maturation of these cells in 3D as well. These findings were confirmed with immunofluorescence stainings on day 21 spheroids for CYP3A4, CD31, CD45 and PDGFRβ for Heps, ECs, iMφ and HSCs respectively. At day 21, spheroids showed decreased expression of HSC activation markers and increased expression of markers specific for quiescence, such as respectively COL1A1 and LRAT, suggesting that the iHSCs become more quiescent in these co-cultures. To mimic fibrosis, we either directly (TGF-β) or indirectly (APAP) induced iHSC activation. Both conditions led to a significant increase of HSC activation marker genes (ACTA2, COL1A1, LOXL2) indicating functionality of both iHSCs and iHeps. Lastly, our iPSC model was compared to spheroids consisting of freshly isolated primary human liver cells. Gene expression levels of cell type-specific markers such as CYP3A4 and PDGFRβ at day 7 of primary liver spheroid cultures were similar to day 13 of iPSC liver cultures, suggesting that the iPSC-derived liver spheroid culture is an adequate in vitro human liver model. Comparisons of cytotoxicity in iPSC versus primary human liver spheroids, induced by APAP and other compounds are still ongoing.
Conclusions: We have established a robust human iPSC-derived liver culture model that can be used to mimic fibrosis in vitro as a replacement of primary human 3D models. This model can be used to investigate pathways involved in fibrosis development and to identify new targets for chronic liver disease therapy.

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PREVALENCE OF CHRONIC HEPATITIS E INFECTION IN IMMUNOSUPPRESSED PATIENTS IN BELGIUM.
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Introduction: Hepatitis E virus (HEV) is now considered as the commonest cause of acute viral hepatitis in Western countries, especially genotype 3 and 4. In immunocompromised patients, chronic HEV have been described, leading in certain cases to cirrhosis, decompensation and death or liver transplantation. A recently published study from the UK based on a Markov cohort model suggests that routine screening for HEV in solid organ transplant (SOT) is very likely to be cost-effective, even more in patients with abnormal transaminases. No data are available on the real prevalence and incidence of HEV chronic infections in this population in Belgium.
Aim: To determine the prevalence of HEV in immunosuppressed populations (SOT and patients suffering from hematological diseases) in a single tertiary center in Belgium, Cliniques universitaires Saint-Luc (CUSL), in Brussels.
Methods: From May 2022 to April 2023, we are prospectively screening for HEV all patients transplanted from a liver, kidney, or heart as well as patients suffering from a lymphoma or followed in the hematology department for a bone marrow transplantation and under immunosuppression from at least three months. The screening includes HEV IgG, HEV IgM and PCR with a genotyping if PCR is positive. Collected data include demographic data, past medical history, reason for immunosuppressive therapy and type of immunosuppressive therapy, routine clinical examination and routine blood test including liver function tests.
Results: We present here an intermediate analysis of a 5-months screening. Among 431 patients, 153 were followed for kidney transplantation, 123 for heart transplantation, 110 for liver transplantation and 45 for hematological pathology requiring maintenance immunosuppression. The median age is 60. The sex ratio F/M is 1/2. The IgG HEV seroprevalence is 9,8% in the whole population, 8,7% in kidney transplanted patients, 12,8% in heart transplanted patients, 12,5% in liver transplanted patients and 0% in hematological pathology. A positive HEV PCR was found in 4 patients, all kidney transplanted, and genotype 3c was identified in all of them. They all presented positive HEV IgG and IgM. At the time of the diagnosis, they were all receiving an immunosuppression based on corticosteroids, a calcineurin inhibitor and mycophenolate mofetil. Only one of them had normal liver function tests at diagnosis. For two of them, the HEV PCR remained positive after 3 months and chronic HEV was diagnosed.
Conclusions: The IgG HEV seroprevalence in our population is 9.8%. In the flemisch blood donor population in 2015, the prevalence was 8,71% and in the serum bank between 2006 and 2014, the prevalence was 4,1% et 5,8%, respectively. HEV PCR was only detected in renal transplanted recipients. More data are awaiting to draw conclusions

on the importance of systematic screening in these immunosuppressed populations. This study is supported by a Gilead fellowship grant.

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THE PAN-PPAR AGONIST LANIFIBRANOR IMPROVES INCREASED PORTAL PRESSURE, ENDOTHELIAL DYSFUNCTION AND LIVER HISTOLOGY IN A RAT MODEL OF EARLY NAFLD. S. Chotkoe (1), Y. Liu (2), G. Wettstein (3), J. Junien (3), L. Vonghia (4), H. Ceuleers (2), J. De Man (2), B. De Winter (1), W. Kwanten (4), S. Francque (4) / [1] Universiteit Antwerpen / Antwerp University Hospital, WILRIJK (Antwerpen), Belgium, Laboratory of Experimental Medicine and Paediatrics, [2] University of Antwerp, Antwerp, Belgium, Laboratory of Experimental Medicine and Paediatrics, [3] Inventiva Pharma, Daix, France, Biology and Pharmacology, [4] Universiteit Antwerpen / Antwerp University Hospital, WILRIJK (Antwerpen), Belgium, Gastroenterology & Hepatology.

Introduction: Non-alcoholic fatty liver disease (NAFLD) is currently the most prevalent chronic liver disease worldwide, with no pharmacological therapy licensed yet. We previously demonstrated an increased intrahepatic vascular resistance (IHVR) related to endothelial dysfunction and an altered endothelin-1 (ET-1) pathway in early NAFLD in rats, potentially contributing to disease progression. The pan-peroxisome proliferator-activated receptor (pan-PPAR) agonist Lanifibranor has demonstrated beneficial effects on liver histology in NAFLD patients and was also shown to have favourable effects in preclinical models of cirrhosis and portal hypertension.
Aim: This study aimed to determine the effects of Lanifibranor on the functional intrahepatic vascular alterations and on the histological features in early NAFLD in a preventive set-up in rats.
Methods: Male Wistar rats (n=8 per group) were fed a methionine-choline-deficient diet (MCD) or control diet (CD) for 4 weeks and received simultaneously vehicle or 100 mg/kg Lanifibranor daily via oral gavage QD. In vivo haemodynamics and blood pressures of the carotid artery, portal vein and inferior caval vein were measured, followed by in situ ex vivo liver perfusion in the same animal to assess baseline transhepatic pressure gradient (THPG) at different flows (flow range 10 -50 mL/min). Dose-response curves were subsequently generated with vasoconstrictors ET-1 (dose range 10^-12–3.10^-9 M) and methoxamine (Mx, 10^-6–3.10^-4 M), and vasodilator acetylcholine (ACh, 10^-6–10^-3 M) after Mx preconstriction (at a dose of 3.10^-5 M). Haematoxylin-Eosin (HE) and Sirius red staining was performed on liver tissue for histological examination using the steatosis-activity- fibrosis (SAF) score.
Results: In vehicle-treated animals, livers of MCD rats showed severe, grade 3 steatosis, without inflammation or fibrosis, compared to normal livers in CD rats. Moreover, MCD rats showed a significantly increased portal pressure in vivo compared to CD rats (5.64±0.63 vs. 3.52±0.24 mmHg, $p<0.0001$), and THPG ex vivo was increased as well at every perfusion flow velocity (e.g., at 30 mL/min: 8.78±0.35 vs. 6.73±0.28 mmHg) with $p<0.001$. Furthermore, the MCD rats were significantly hyperreactive to ET-1 and Mx, and hyporeactive to Ach compared to their CD counterparts. Treatment with Lanifibranor induced no changes of in vivo and ex vivo THPG measurements in CD rats, but significantly decreased the portal pressure in vivo (from 5.64±0.63 to 3.08±0.28 mmHg, $p<0.0001$) as well as THPG ex vivo at all flows (e.g., at 30 ml/min: from 8.78±0.35 to 6.31±0.15 mmHg, $p<0.001$) in MCD rats. Lanifibranor improved the hyperreactivity to Mx and tended to improve the hyporeactivity to ACh in MCD rats, although it did not normalise ET-1 hyperreactivity. Histology confirmed that Lanifibranor also improved steatosis in MCD rats compared to vehicle, mainly in the pericentral zones.
Conclusions: The pan-PPAR agonist Lanifibranor substantially reduces the increased portal pressure and related functional intrahepatic vascular alterations associated with early NAFLD. Lanifibranor improves liver histology as well. These data further support the role of intrahepatic vascular alterations in the development in NAFLD and NAFLD-related portal hypertension on the one hand, and the potential of Lanifibranor as treatment for NAFLD on the other hand. A complementary study with the same experimental set-up was performed to unravel the individual contribution of each PPAR isotype (alpha, delta and gamma) to the beneficial effects of Lanifibranor.

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EXCESSIVE PROLIFERATION AFTER EXTENDED HEPATECTOMY COMPROMISES LIVER FUNCTION IN MICE. M. De Rudder (1), I. Leclercq (2), A. Dili (3) / [1] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, Laboratory of Hepato-Gastroenterology, [2] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, Laboratory of Hepato-gastroenterology, [3] Centre Hospitalier Universitaire Mont-Godinne, Belgium, HPB surgery unit.

Introduction: Small for size syndrome (SFSS) is a post- extended hepatectomy liver failure. Hepatocyte hyperproliferation and vascular damage are thought to be the two major culprits leading to organ failure. In previous studies from the lab, we showed that exposure to hypoxia prevented mortality in mice after an extended hepatectomy. Higher survival rates were associated with an early trigger of endothelial cell proliferation and subsequently a denser sinusoidal network with larger sinusoids, rescue of the disturbed perfusion found after a SFSS-setting hepatectomy, and recruitment of endothelial progenitor cells. Surprisingly, decreased hepatocyte proliferation was associated with survival. Here we

tested 2 propositions: 1) That early stimulation of vasculogenesis is key for the prevention of liver failure after extended hepatectomy. 2) That hepatocytes massively undergo Epithelial to Mesenchymal Transition which is favorable to proliferation but compromises hepatocyte function, leading to liver failure.
Aim: In this study, we want to assess if administration of G-CSF in order to manage vascular damage induced by a SFSS-setting hepatectomy can rescue survival. We also want to assess if hepatocytes engage in an EMT process after an extended hepatectomy and evaluate whether this would jeopardize liver function for proliferation in the liver remnant.
Methods: G-CSF administration consisted of 3 peritoneal injections (2 the day before the surgery and one at the time of surgery). Vascular diameter and density were assessed on CD31 staining. Recruitment of endothelial progenitors was assessed using Cdh5-CreERT2 x mTmG mice, expressing GFP in mature endothelial cells when tamoxifen is administered. Liver function was evaluated by qPCR for the xenobiotic metabolism, circulating factor V by ELISA, circulating albumin by colorimetric test and hepatocyte glycogen content by PAS staining. EMT was evaluated by expression of E-Cadherin by immunofluorescence, and gene expression of HNF4A and Snai1 by qPCR. EMT pathway was investigated via immunofluorescence of Hes1 and Notch1.
Results: Administration of granulatory-colony stimulation factor (G-CSF) increased vascular diameter and density and induced the recruitment of endothelial progenitors in regenerating livers compared to non-treated animals. Despite managing vascular defects, administration of G-CSF did not rescue survival. We thus focused on the hepatocyte population. After a SFSS-setting hepatectomy, a large portion of the hepatocytes enters the cell cycle at the same time (around 50% at POD3), especially in peri-portal and peri-central areas, where key metabolizing functions are performed. High proliferation was associated with significantly decreased circulating albumin and factor V, two proteins heavily produced by the liver. Xenobiotic metabolism genes CYP1A2 and CYP2E1 were also decreased in normoxia compared to hypoxia. Finally, PAS staining revealed that only 30% of hepatocytes were PAS+, compared to 60% in mice kept in hypoxia. Loss of epithelial characteristics and in this case hepatocyte signature is a sign of EMT. HNF4A, a master regulator of hepatocyte phenotype, was downregulated in normoxia and its expression was inversely correlated with Snai1, a regulator of EMT. Concordantly, the epithelial marker E-Cadherin was faintly stained in mice kept in normoxia. Finally, we explored through which pathway EMT is induced in hepatocytes. Notch1 intracellular domain was stained inside the nucleus of hepatocytes of mice kept in normoxia while no nuclear staining was found in hypoxia. Similarly, Hes1, a target of the Notch pathway, was more expressed in normoxia compared to hypoxia.
Conclusions: In this study, we found that vascular damage after a SFSS-setting hepatectomy are rescued by administration of G-CSF. However, this was not sufficient to increase survival. Focusing on hepatocytes, we found that SFSS-setting hepatectomy leads to extravagant engagement in the cell cycle in hepatocytes, and this was associated with decreased function of the liver remnant. We found that a large portion of the proliferative hepatocytes engaged in an EMT process through the Notch1/Hes1 pathway. Thus, we think that EMT engagement after a SFSS-setting hepatectomy disrupts the balance between function and proliferation in the remnant, leading to organ failure.

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ALVEOLAR ECHINOCOCCOSIS IS INCREASING IN SOUTHERN BELGIUM: A REPORT OF THE BELGIAN NATIONAL REFERENCE LABORATORY FOR ECHINOCOCCOSIS (BNRLE) AND CLINICAL EXPERIENCE OF ECHINO-LIEGE. O. Detry (1), C. Bihain (2), R. Sacheli (3), S. Egrek (4), N. Blétard (5), P. Meunier (6), P. Lovinfosse (7), J. Delwaide (8), N. Botembe (9), E. Larranaga (10), C. Truyens (11), B. Delaere (12), B. Pirotte (13), J. Giot (14), P. Leonard (14), M. Hayette (3) / [1] Centre Hospitalier Universitaire de Liège, Liège, Belgium, ECHINO-Liege, Dpt of Abdominal Surgery and Transplantation, [2] CHU of Liège, Belgium, Dpt of Abdominal Surgery and Transplantation, [3] CHU of Liège, Belgium, ECHINO-Liege, Dpt of Clinical Microbiology, Belgian National Reference Laboratory for Echinococcosis, (BNRLE), [4] CHU of Liège, Belgium, Dpt of Clinical Microbiology, Belgian National Reference Laboratory for Echinococcosis, (BNRLE), [5] CHU of Liège, Belgium, ECHINO -Liege, Dpt of Pathology, [6] CHU of Liège, Belgium, ECHINO-Liege, Dpt of Radiology, [7] CHU of Liège, Belgium, ECHINO-Liege, Dpt of Nuclear Medicine, [8] CHU of Liège, Belgium, ECHINO-Liege, Dpt of Hepatogastroenterology, [9] Centre Hospitalier des Ardennes, Libramont, Belgium, Dpt of Gastroenterology, [10] Erasme Hospital, Brussels, Belgium, Dpt of Infectiology, [11] Université Libre de Bruxelles Faculté de Médecine, Brussels, Belgium, of Parasitology, [12] CHU Dinant Godinne, Yvoir, Belgium, Dpt of Infectiology, [13] CHR Citadelle, Liège, Belgium, ECHINO-Liege, Dpt of Infectiology, [14] CHU of Liège, , Belgium, ECHINO-Liege, Dpt of Infectiology.

Introduction: Alveolar echinococcosis (AE) is endemic in Southern Belgium where up to 50% of the red foxes might be infected and spread Echinococcus eggs in the environment. In humans, the primary target organ of AE is the liver, in which AE grows as a parasitic tumor and might later develop in other organs as a malignancy and be lethal. In response to the increasing number of AE cases, a multidisciplinary group (ECHINO-Liege) was created in CHU Liege to improve AE management and to discuss the AE cases. In addition, on the top of a retrospective AE registry, ECHINO-Liege is prospectively building a database (ECHINO-Base) and a biobank (ECHINO-Bank) of AE patients managed in CHU Liege, after EC approval and informed consent. Finally, since 2021, the Belgian National Reference Laboratory for Echinococcosis (BNRLE) is based in the department of Clinical Microbiology of CHU Liege.

Aim: The aim of this study was to report the actual epidemiological and clinical situation on AE in Belgium, using the BNRLE data and the clinical experience of ECHINO-Liege.
Methods: All Belgian clinical laboratories were asked to fill epidemiological forms on AE cases detected in 2021 and 2022. All cases confirmed by serology (immunoblot) and/or PCR and/or histology (proved cases) or without microbiological confirmation (probable and possible cases) were included. These cases were added to the retrospective series already published in 2018 and to the cases discussed during the regular meetings of ECHINO-Liege.
Results: AE was newly diagnosed and reported to BNRLE in 16 patients in the time-period of 2 years, added to the 36 patients previously registered (total: 52 patients, 29M/23F) (mean age: 60y, 19-89). Most patients were born and lived in Wallonia or the Brussels area. All cases but 2 are considered contracted in Belgium (1 in France and 1 in Luxembourg). 31 patients underwent liver resection and 1 liver transplantation.
Conclusions: AE appears to be spreading in Southern Belgium. The authorities should be aware of this public health issue. The radiologists and gastroenterologists should be informed of this diagnosis possibility in case of liver tumor. A national multicentric survey will be soon initiated as a collaboration between the different hospitals in the whole country.

- A26 -

THE SILENCING OF SOX9 INHIBITS THE DUCTULAR REACTION EXPANSION BUT ENHANCES THE DIFFERENTIATION OF DR CELLS INTO HEPATOCYTES IN THE DISEASED LIVER. A. de Schaetzen (1), M. De Rudder (1), A. Pottier (2), I. Leclercq (1) / [1] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, Hepato-Gastro-Enterology, [2] Université catholique de Louvain (UCLouvain), Belgium, Hepato-Gastro-Enterology.

Introduction: After acute damage or liver resection the liver regenerates and each cell compartment proliferates to repopulate the cells that were lost. In chronic liver disease, hepatocytes are found in a state of replicative senescence and are no longer able to proliferate. In such a setting, cholangiocytes proliferate and invade the parenchyma, in a phenomenon called the ductular reaction (DR). Cells of the ductular reaction are in transitional shift between cholangiocytes and hepatocytes, and have the ability to differentiate in hepatocytes, offering an alternative path for regeneration. Observations in animal models show nevertheless that DR cells generate only a modest fraction of hepatocytes. Hence strategies to enhance DR-derived regeneration are needed to significantly support liver function in chronic diseases. Sox9 is a transcription factor that determines the biliary fate of the bipotential precursor to cholangiocytes and hepatocytes during embryogenesis. Sox9 ectopic expression is proposed to direct liver epithelial cells towards the biliary lineage. Here we hypothesize that the silencing of Sox9 in cells of the ductular reaction will ease their shift towards the hepatocyte lineage, thereby enhancing their contribution to liver regeneration.
Aim: We aim to enhance DR cell-to-hepatocyte differentiation by silencing Sox9 in biliary cells.
Methods: We made successive crossings to obtain OpniCreERT2 : Rosa26RYFP : Sox9floxed transgenic mice. In these mice, the injection of Tamoxifen drives the constitutive expression of YFP and the silencing of Sox9 in cholangiocytes alone. Any cell expressing YFP is a cholangiocyte or its progeny. Sox9Chol KO and controls with intact Sox9 expression received carbon tetrachloride (CCl4) 3 times per week for 6 weeks to cause chronic hepatocellular damage. In a separate experiment, we first treated mice with CCl4 to induce DR and then operate Sox9 silencing in cholangiocytes, then mice underwent a 2 weeks recovery period before harvest. We used immunohistochemistry and immunofluorescence (IF) to quantify the number of biliary cells in which Tamoxifen induced YFP expression and Sox9 silencing, and to investigate the effect of the silencing of Sox9 on DR-driven regeneration.
Results: In response to tamoxifen injection, we observed the expression of YFP in 71% (±1,9 %) of cholangiocytes together with expression of Sox9 in none of them in Sox9chol KO mice. In controls mice 82% (±3,5%) of cholangiocytes expressed YFP and all of them expressed Sox9. After 6 weeks of CCl4, the magnitude of the ductular reaction, as measured by the area of Ck19+ cells, was significantly lower in Sox9Chol KO than in controls. Patches of YFP+/HNF4α+ hepatocytes generated from the DR were present in all animals, but similar in density in Sox9Chol KO and in controls, this regardless whether the ductular reaction was weak (Sox9Chol KO) or vigorous (controls). This supports that Sox9 deletion favors differentiation of DR cells. To further support this, we silenced Sox9 after the induction of the DR in chronic hepatocellular injury, and examined livers after a 2 weeks recovery period. We confirmed that tamoxifen injection effectively induced YFP expression and silenced Sox9 in 68% and 100% of DR cells respectively in Sox9Chol KO and in 83% and 0% of DR cells in controls. The number of YFP+ hepatocytes was significiantly increased in Sox9Chol KO compared to controls.
Conclusions: We generated a model for inducible and cholangiocyte-specific YFP expression along with Sox9 silencing: the OpniCreERT2 : Rosa26RYFP : Sox9floxed mice. With this model, we showed that the silencing of Sox9 impairs the expansion of DR cells. Furthermore, the silencing of Sox9 in DR cells enhances their hepatocytic differentiation.

- A27 -

NODULAR REGENERATIVE HYPERPLASIA OF THE LIVER : AN INSIGHT INTO THE EPIDEMIOLOGY AND THE CLINICAL CHARACTERISTICS OF A RARE AND POORLY UNDERSTOOD ENTITY. E. Kaze (1),

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Introduction: Recently, the Vascular Liver Disease Interest Group (VALDIG) proposed the new term porto-sinusoidal vascular disorder to include different conditions sharing three specific histological lesions: obliterative portal venopathy, incomplete septal cirrhosis and nodular regenerative hyperplasia (NRH). However, little is known about the clinical significance of these lesions as well as the outcome of these patients.
Aim: The aim of this study was to describe the epidemiology and the clinical characteristics of patients with a histopathologic diagnosis of NRH.
Methods: From January 2015 to March 2021, adult patients with a histopathologic diagnosis of NRH were included. They were extracted from the database of the pathology department of Cliniques universitaires Saint-Luc, Brussels. Baseline characteristics, conditions associated with NRH, clinical and laboratory findings at diagnosis were recorded. Complications of portal hypertension and mortality were analyzed during a 1 to 6-year follow-up.
Results: Our study included 100 patients with a histopathologic diagnosis of NRH from January 2015 to March 2021. Liver tissue was obtained by transjugular liver biopsy (52%), percutaneous liver biopsy (21%), liver resection specimen (25%) or by intraoperative liver biopsy (2%). There were 55 men and 45 women. The indications for liver tissue sample were diagnostic evaluation of portal hypertension (32%), abnormal liver tests (25%), liver resections for metastasis (22%) , protocol biopsies after liver transplantation (12%) and others (9%). 44% had clinical features of portal hypertension at histological diagnosis (splenomegaly, oesophageal or gastric varices). Conditions related to NRH were immunosuppressive status (62%), cardiovascular diseases (6%), genetic diseases (4%), and autoimmune/inflammatory conditions (4%). No associated conditions could be identified in 24% of the cases. We selected patients in whom liver tissue was obtained during the evaluation of clinical and biological signs of portal hypertension or abnormal liver tests (group 1, n = 57). Among them, 5 patients were excluded due to missing data. The remaining patients were compared with patients who had an incidental histologic diagnosis of NRH (group 2, n = 34) : patients undergoing liver resection for metastasis (n=22) and patients with protocol biopsies after liver transplantation (n=12). We excluded 8 patients who had a protocol liver biopsy after transplantation because of abnormal liver tests. 9 patients in whom the diagnosis of NRH was made in another setting were not included in the analysis. Compared to patients with clinical manifestations (group 1), patients with incidental diagnosis of NRH (group 2) had more often an immunosuppressive status (drug or disease related) (100% versus 40%, $p<0.01$), were more often treated by oxaliplatin (69% versus 2%, $p<0.01$) and developed less manifestations of portal hypertension during follow-up (0% versus 31% ($p<0.02$). Liver-related mortality was 2% in group 1 compared to 0% in group 2.
Conclusions: Our study shows that NRH is a unique histologic lesion associated to different clinical manifestations: about 50% of patients presented signs of portal hypertension or abnormal liver tests. Oxaliplatin treatment was frequently associated to NRH (20% of patients). Notably, the majority of patients with NRH related to oxaliplatin didn't experience liver-related complications.

- A28 -

UNRAVELING THE INDIVIDUAL CONTRIBUTIONS OF THE PPAR ISOTYPES TO THE PAN-PPAR AGONIST LANIFIBRANOR-INDUCED IMPROVEMENTS OF THE VASCULAR ALTERATIONS AND LIVER HISTOLOGY IN A RAT MODEL OF EARLY NAFLD

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is currently the most prevalent chronic liver disease worldwide, with no pharmacological therapy licensed yet. The pan-peroxisome proliferator-activated receptor (pan-PPAR) agonist Lanifibranor has demonstrated beneficial effects in NAFLD and preclinical models of cirrhosis and portal hypertension. In a previous study we showed that in a preventive set-up Lanifibranor improves the increased intrahepatic vascular resistance (IHVR), the related endothelial dysfunction and the associated liver histology in a rat model of early NAFLD. The PPAR receptors consists of 3 isotypes (alpha, delta and gamma), differentially expressed across tissues and operating through a complex physiological interplay.
Aim: This study aimed to provide more insights in the underlying mechanism through which Lanifibranor acts on the functional intrahepatic vascular alterations and on the histological features in early NAFLD, by exploring the mono-PPAR agonists GW501516 (PPAR-delta agonist) and Rosiglitazone (PPAR-gamma agonist) in the same experimental set-up as before with 100 mg/kg Lanifibranor using a rat model of early NAFLD.
Methods: Male Wistar rats (n=8 per group) were fed a methionine-choline-deficient diet (MCD) or control diet (CD) for 4 weeks simultaneously with either vehicle, 10 mg/kg GW501516, or 5 mg/kg Rosiglitazone treatment via oral gavage daily QD. In vivo haemodynamics and blood pressures of the carotid artery, portal vein and inferior caval vein

were measured, followed by in situ ex vivo liver perfusion in the same animal to assess baseline transhepatic pressure gradient (THPG) at different flows (flow range 10 -50 mL/min). Dose-response curves were subsequently generated with the vasoconstrictors endothelin-1 (ET-1) and methoxamine (Mx), and the vasodilator acetylcholine (ACh) after Mx preconstriction. Haematoxylin-Eosin (HE) and Sirius red staining was performed on liver tissues for histological examination using the steatosis - activity - fibrosis (SAF) score.
Results: In vehicle-treated animals, livers of MCD rats showed severe, grade 3 steatosis, without inflammation or fibrosis, compared to normal livers in CD rats. MCD rats showed a significantly increased portal pressure in vivo compared to CD rats (5.64±0.63 vs. 3.52±0.24 mmHg, $p<0.0001$), and THPG ex vivo was increased as well at every perfusion flow velocity (e.g., at 30 mL/min: 8.78±0.35 vs. 6.73±0.28 mmHg) with $p<0.001$. Furthermore, the MCD rats were significantly hyperreactive to ET-1 and Mx, and hyporeactive to ACh compared to CD rats. GW501516 significantly decreased portal pressure in vivo (from 5.64±0.63 to 4.34±0.16 mmHg, $p<0.0001$), and THPG ex vivo (e.g., at 30 mL/min: from 8.78±0.35 to 7.61±0.34 mmHg) with $p<0.01$ in MCD rats, however, both to a lesser extent than Lanifibranor. It improved the hyperreactivity to Mx, similar to Lanifibranor, and tended to improve ET-1 hyperreactivity whereas Lanifbranor did not. GW501516 was unable to normalise ACh hyporeactivity in contrast to Lanifibranor. Finally, histology showed that Lanifibranor caused amelioration of steatosis, but GW501516 only weakly decreased steatosis. Rosiglitazone significantly decreased portal pressure in vivo (from 5.64±0.63 to 4.43±0.27 mmHg, $p<0.0001$), and it decreased THPG ex vivo as well in MCD rats (e.g., at 30 mL/min: from 8.78±0.35 to 7.95±0.28 mmHg, $p=0.043$), though less than Lanifibranor did. It also slightly increased THPG ex vivo in CD rats, however only significant at a flow of 50 ml/min (12.01±0.35 vs. 10.65±0.48 mmHg, $p=0.013$) compared to vehicle-treated CD rats. In MCD rats Rosiglitazone improved the hyperreactivity to Mx, tended to improve ACh hyporeactivity, but did not normalise ET-1 hyperreactivity, similar to the observations with Lanifibranor. Further, Rosiglitazone caused only minimal histological improvement of steatosis in MCD rats.
Conclusions: The mono-PPAR agonists GW501516 and Rosiglitazone both reduce the increased portal pressure and related functional vascular intrahepatic alterations associated with early NAFLD. Both also minimally improved steatosis. However, all changes were less pronounced than the net effect of Lanifibranor. These data suggest that there is an additive effect of combined PPAR agonism compared to mono-agonism to the vascular alterations in early NAFLD. The contribution of PPAR-alpha is still under investigation.

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FIBROSIS STAGE IS THE MAIN DRIVER OF LIVER-RELATED EVENTS IN ADULTS WITH BIOPSY- PROVEN NONALCOHOLIC FATTY LIVER DISEASE. A. Bocquillon (1), L. Otero Sanchez (1), D. Degré (1), A. Lepida (1), A. Putignano (1), N. Boon (1), T. Gustot (1), E. Trépo (1), C. Moreno (1) / [1] Erasme Hospital, Brussels, Belgium, Gastroenterology, Hepato-Pancreatology and Digestive Oncology

Introduction: Patients with Non-alcoholic Fatty Liver Disease (NAFLD) have a greater risk of hepatic decompensation and a higher overall mortality rate than the general population. Risk factors associated with these complications and mortality are not well established.
Aim: Our aim was to study overall mortality and risks factors associated with liver related events and mortality in patients with biopsy-proven NAFLD.
Methods: We conducted a single-center retrospective study including 228 patients with biopsy proven NAFLD, performed at Erasme Hospital in Belgium between 2009 and 2019. The main inclusion criteria were: ≥18 years old, biopsy-proven NAFLD (≥5% macrovesicular steatosis); exclusion criteria were: other causes of chronic liver diseases, excessive alcohol consumption (>20 g of alcohol/day for women and >30 g/day for men). We studied the incidence of liver-related events (LRE [hepatocellular carcinoma, clinical apparent ascites, hepatic encephalopathy, variceal hemorrhage]) and their associated risk factors using Fine and Gray competing risk model. Risk factors associated with mortality were studied using COX regression.
Results: A total of 228 patients, 109 men (48%) and 119 women (52%) with a median age of 63 years were included. Patients were followed for a median of 2,7 years (0,57-6,00). 83 patients (36%) had NAFLD without NASH (NAS 1-2), 95 patients (42%) had borderline NASH (NAS 3-4) and 50 patients (22%) had NASH (NAS≥5). Cardiovascular events occurred in 9,57% of the patients during the study period (30% myocardial infarction, 30% stroke and 30% acute hearth failure). The main causes of mortality were cardiovascular events (25%) and infections (11%). LRE increased with fibrosis stage (2,3% at 10 years for F0-F2 vs 17,5% at 10 years for F3-F4). It should be noted that all the patients with a LRE were diabetic. Risk factors associated with LRE were: age ($p=0.016$), GGT ($p<0.001$), PAL ($p<0.001$), bilirubin ($p<0.001$), HbA1c ($p<0.001$), NAS-score ($p=0.014$) and fibrosis stage F3-F4 ($p=0.022$). In the multi-state model, only fibrosis stage F3-F4 remains a significant risk factor (HR=6.95, $p=0.015$). Risk factors associated with mortality were: HTA ($p=0.041$), ALT ($p=0.023$), GGT ($p<0.001$), albumin ($p<0.001$), HDL-cholesterol ($p=0.027$) and LDL-cholesterol ($p=0.032$). The multi- state model included GGT, PAL, albumin, LDL- cholesterol and ALT.
Conclusions: In this cohort of biopsy-proven NAFLD patients, we confirmed that the first cause of death in NAFLD is related to cardiovascular events. Advanced fibrosis and cirrhosis are the main risk factors of liver-related events.

These results highlight the importance of systematic cardiovascular screening in this population and identify the target population for follow-up by the liver specialist.

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FRUCTOSE AND GLUCOSE SUPPLEMENTATION FOR THE DEVELOPMENT OF NAFLD AND NASH IN MICE. L. Cools (1), A. Dumarey (1), H. Reynaert (1), S. Verhulst (1), L. van Grunsven (1) / [1] Vrije Universiteit Brussel (VUB), Jette, Belgium, BMWE-LIVR.

Introduction: Non-alcoholic fatty liver disease (NAFLD) includes both the benign form of non-alcoholic fatty liver (NAFL) characterized by simple steatosis and the more severe form non-alcoholic steatohepatitis defined by steatosis, inflammation and hepatocyte ballooning with or without fibrosis with possible progression to hepatocellular carcinoma. Many dietary animal models have been developed, based on the administration of fat (from 45%-75% of total calories) and are able to induce obesity and steatosis in 24 weeks. As for the induction of inflammation and fibrosis it can take up to a year which makes this very costly and time consuming. To speed up the progression towards NASH, a study of Tsuchida et al. (J.Hepatology, 2018) showed that the co-administration of a high fat diet supplemented with a very low dose of fructose and glucose in tap water together with a weekly intraperitoneal (i.p.) injection of a low dose of carbon tetrachloride results in a NAFL and NASH phenotype in 12 weeks in C57BL/6J mice. As the consumption of fructose and glucose in beverages has increased in the last couple of years, many studies have shown the correlation of these sugars in the development of NAFLD (Jensen, J. Hepatology, 2018).
Aim: The goal of this study was to investigate whether we could model NAFL and NASH by the administration of only fructose and glucose in tap water of male Balb/C mice combined with a weekly i.p. injection of CCl4.
Methods: 40 male Balb/C mice were divided in 4 experimental groups. The Ctrl group received regular chow and tap water for 10 weeks and a weekly i.p. injection of mineral oil (solvent of CCl4). The fibrotic Ctrl group received regular chow and tap water for 10 weeks together with a weekly CCl4 i.p. injection (0,32µg/g body weight). The NAFL group received regular chow and 20% fructose and 20% glucose rich tap water for 10 weeks combined with a weekly oil injection. For NASH induction, mice received regular chow and 20% fructose and 20% glucose rich tap water and a weekly injection of i.p. injected CCl4 (0,32µg/g body weight) for 10 weeks. Cryosections were stained with Oil Red O for the assessment of fat accumulation. Picrosirius was performed on paraffin sections for fibrosis visualization. Fluorescent stainings for αSMA and F4/80 were performed on paraffin sections for assessment of HSC activation and Kupffer cell presence and imaged with an EVOS M7000.
Results: Male mice developed a NAFL phenotype after 10 weeks of fructose and glucose rich drinking water confirmed by Oil Red O staining. The co-treatment with a weekly low dose of i.p. injected CCl4 resulted in a higher body weight (NASH mice 35,06g ±2,03g vs Ctrl mice 33,01g ±2,46g) and liver weight (NASH mice 2,75g ±0,26g vs Ctrl mice 1,86g ±0,21g) in mice, a significant increase in intrahepatic fat accumulation confirmed with Oil Red O and fibrosis development shown by Picrosirius and αSMA stainings as compared to the Ctrl group. Furthermore, an increase in F4/80 positive cells was seen in the NASH group as compared to Ctrl indicative of a NASH phenotype.
Conclusions: We show that only fructose and glucose administration in drinking water of Balb/C mice results in intrahepatic fat accumulation in only 10 weeks. When combined with an accelerator, here a weekly low dose of CCl4 , this results in the progression towards a NASH phenotype shown at histological and immunological levels. RNA sequencing analysis is ongoing, comparing this model to previously published models of mice receiving high fat diets.

- B01 -

EOSINOPHILS EXERT A PRO-INFLAMMATORY ROLE IN A CHRONIC DSS COLITIS MODEL WITHOUT AN IMPACT ON FIBROSIS. I. Jacobs (1), S. Deleu (2), J. Cremer (2), G. De Hertogh (3), S. Vermeire (2), C. Breynaert (4), B. Verstockt (2), T. Vanuytsel (2) / [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, [3] KUL - University of Leuven, Leuven, Belgium, Department of Imaging and Pathology, [4] KUL - University of Leuven, Leuven, Belgium, Department of Microbiology, Immunology and Transplantation.

Introduction: Eosinophils might play a pro-inflammatory role in inflammatory bowel disease (IBD). However, the role of eosinophils in intestinal fibrosis remains poorly understood, although a pro-fibrotic function has been hypothesized based on data outside the gastrointestinal tract.
Aim: Therefore, we aimed to unravel the role of eosinophils in chronic intestinal inflammation and fibrosis and to explore eosinophil depletion as a potential therapeutic target.
Methods: A 3-cycles chronic dextran sodium sulphate (DSS) model was induced in 6-8-week-old C57BL/6 wild type mice. Mice received 3 DSS cycles (1.5% - 2.00% - 2.00%) in which 1 DSS cycle consisted of 1 week of DSS administration followed by 2 weeks of recovery. During the 3 cycles, and starting 3 days prior to colitis induction, anti-CCR3 antibody or isotype injections were given twice weekly to study the effect of the eosinophil depletion (total of 18 injections). The disease activity index (DAI; weight loss, stool consistency and presence of blood) was determined twice weekly as well. At sacrifice, colonic damage was scored macroscopically (presence of hyperaemia, adhesions and length and degree of colon affected by inflammation) and colonic single cells were isolated and fluorescently stained for flow cytometry. Eosinophils were thereby identified as CD45+ CD11b+ Siglec-F+ CD117- cells. Lastly, a histological active disease score was determined comprising of the sum of neutrophil infiltration, mononuclear cell infiltration, changes in mucosal architecture, goblet cell loss and epithelial defects (Creyns et al., 2019). Intestinal fibrosis was assessed via colon weight/length ratio, COL1A1 gene expression and collagen deposition with a Martius Scarlet Blue (MSB) staining and a colorimetric hydroxyproline assay.
Results: Blood (0.2 ± 0.2 vs 0.7 ± 0.3 % of CD45+ cells) and colonic (0.4 ± 0.4 vs 6.6 ± 4.6 % of CD45+ cells) eosinophil depletion via anti-CCR3 injections was confirmed via flow cytometry. The DAI in the eosinophil depleted group was decreased compared to the isotype injected group (area under the curve 115.4 ± 29 vs 160.6 ± 28; p=0.02). A similar trend was seen in the macroscopic damage score (2.0 ± 1.3 vs 3.9 ± 2.1; p=0.08). Furthermore, a lower histological active disease score was found in the mice in which the eosinophils were depleted compared to the isotype injected mice (8.8 ± 0.8 vs 12.8 ± 1.5; p=0.002). Lastly, no differences in the parameters for fibrosis between the anti-CCR3 injected and isotype injected groups were observed.
Conclusions: Eosinophil depletion via intraperitoneal anti-CCR3 injections resulted in partial protection from intestinal inflammation in chronic DSS and could therefore be further explored as a potential therapeutic agent. In contrast, eosinophil depletion does not seem to have any anti-fibrotic effect.

- B02 -

DSS-COLITIS INDUCED INTESTINAL BARRIER DYSFUNCTION DEPENDS ON THE MICROBIOME: AN EXPLORATIVE STUDY N. Hanning (1), R. Verboven (2), B. Oosterlinck (1), J. De Man (1), H. De Schepper (3), J. Timmermans (2), A. Smet (1), B. De Winter (1) / [1] University of Antwerp, Antwerp, Belgium, Laboratory of Experimental Medicine and Pediatrics, [2] University of Antwerp, Antwerp, Belgium, Laboratory of Cell Biology and Histology, [3] Antwerp University Hospital, Edegem, Belgium, Gastroenterology and Hepatology.

Introduction: Dextran sodium sulphate (DSS) animal models are frequently used to study intestinal barrier dysfunction in the pathogenesis of inflammatory bowel diseases. However, the role of the gut microbiome in the regulation of intestinal permeability remains to be further elucidated in this experimental model.
Aim: We aimed to explore the role of the gut microbiome in maintaining intestinal barrier function in normal conditions as well as in DSS-induced acute colitis. Furthermore, we investigated whether the effects of DSS on intestinal barrier function and inflammation varied between different regions of the gastrointestinal tract.
Methods: The gut microbiome in 12-week-old female C57Bl6/J mice was depleted by administering a broad-spectrum antimicrobial cocktail via orogastric gavages twice daily for a total of 10 days. Control animals were administered sterile water. Afterwards, mice were exposed to 3% DSS or normal drinking water for 7 days. Subsequently, several assays were performed to quantify intestinal barrier function in the 4 groups (vehicle (VEH) vs DSS, with or without antibiotic pre-treatment (AB/CON), n = 10–11 animals/group). To assess overall intestinal permeability in vivo, mice were given an oral gavage (200 µL) containing 100 mg/mL creatinine or 60 mg/mL 4kDa FITC-dextran. Five hours later, serum samples were obtained; creatinine levels were determined as a marker of pore pathway permeability, while 4kDa FITC-dextran concentrations were quantified as a marker of the leak and unrestricted pathways. Ex vivo Ussing

chamber experiments were performed to assess intestinal barrier function in the distal colon, proximal colon and terminal ileum. To this end, paracellular flux of 4kDa FITC-dextran across full-thickness tissue samples as well as transepithelial electrical resistance (TEER) were measured. Tissue mRNA expression of several tight junction proteins and mucins were quantified by means of RT-qPCR. Finally, myeloperoxidase (MPO) activity and histological scorings were used to evaluate the extent of inflammation in the distal colon, proximal colon and terminal ileum of the 4 different groups.
Results: Microbiome depletion did not disrupt barrier function. However, the response to DSS differed between control and microbiome-depleted animals. In control animals exposed to DSS, the median serum concentration after administration of 4kDa FITC-dextran in vivo was increased fourfold compared to vehicle-treated animals (CON+VEH: 1.20 (0.98 – 1.70) µg/mL vs CON+DSS: 4.97 (2.41 – 8.46) µg/mL, p = 0.003). In contrast, serum concentrations of 4kDa FITC-dextran were not significantly increased following exposure to DSS in microbiome-depleted mice (AB+VEH: 0.99 (0.94 – 1.29) µg/mL vs AB+DSS: 1.72 (1.22 – 2.47) µg/mL, p = 0.092). Surprisingly, exposure to DSS in microbiome-depleted mice resulted in an increased transepithelial transport of creatinine, compared to vehicle-treated animals. Therefore, DSS seems to mainly affect pore pathway permeability but not leak or unrestricted pathway permeability in microbiome-depleted animals. Ussing chamber experiments in control animals revealed that DSS disrupted intestinal barrier function of the distal colon. In particular, the flux of 4kDa FITC-dextran increased (CON+VEH: 1.70 (1.04 – 2.27) µg/hr/cm2 vs CON+DSS: 6.23 (3.25 – 9.35) µg/hr/cm2, p = 0.001), while TEER decreased (CON+VEH: 55.30 (47.55 – 70.42) Ωcm2 vs CON+DSS: 24.53 (18.43 – 26.88) Ωcm2, p = 0.001). Microbiome depletion prevented these DSS-induced changes in the flux of 4kDa FITC-dextran (AB+VEH: 2.56 (1.95 – 3.25) µg/hr/cm2 vs AB+DSS: 2.01 (1.17 – 3.23) µg/hr/cm2, p = 1.000) and TEER (AB+VEH: 43.46 (39.01 – 64.21) Ωcm2 vs AB+DSS: 50.67 (27.66 – 69.16) Ωcm2, p = 1.000). The proximal colon and terminal ileum remained unaffected by DSS, both in control and microbiome-depleted mice. Distinct changes in the expression of tight junction proteins and several mucins were observed in the different treatment groups. Exposure of control mice to DSS resulted in increased inflammatory scores and MPO activity in the distal and proximal colon, while the ileum remained unaffected. A similar pattern was observed in microbiome-depleted animals, but the degree of inflammation was attenuated in these mice.
Conclusions: In healthy mice, depletion of the gut microbiome did not affect intestinal barrier function in the distal and proximal colon or terminal ileum. Microbiome depletion prevented DSS-induced intestinal hyperpermeability of the leak or unrestricted pathway, but not of the pore pathway. In microbiome-depleted animals exposed to DSS, the degree of inflammation was lower than in control mice. Whether the changes in intestinal barrier function precede or follow the inflammatory changes, requires further investigation.

- B03 -

GASTROINTESTINAL TRAITS IN AN ACCELERATED AGING MOUSE MODEL AT BASELINE AND AFTER DSS-INDUCED CHRONIC COLITIS R. Verboven (1), P. Verstraelen (1), S. Van Remoortel (1), N. De Loose (1), N. Hanning (2), B. De Winter (2), S. Ibiza-Martinez (1), W. De Vos (1), J. Timmermans (1) / [1] University of Antwerp, Antwerp, Belgium, Laboratory of Cell Biology and Histology, [2] University of Antwerp, Antwerp, Belgium, Laboratory of Experimental Medicine and Pediatrics

Introduction: Aging and inflammation, two of the most defining risk factors for Alzheimer's disease, compromise the gastrointestinal (GI) barrier. Conversely, patients with inflammatory bowel diseases have an increased risk for developing dementia. This points to a bidirectional communication between the GI tract and its enteric nervous system (ENS), and the CNS. Given their reported neurodegenerative features, we studied GI (dys-)function in an accelerated aging mouse model (Senescence Accelerated Mouse Prone 8; SAMP8) with respect to its healthy counterpart (SAMR1).
Aim: To investigate whether GI function is affected in SAMP8 mice and whether the central neurodegenerative pathology is exacerbated by chronic intestinal inflammation.
Methods: In a first experiment, GI function was assessed in SAMP8 and SAMR1 mice aged 2, 5 and 9 months. To this end, GI transit was quantified by collection of fecal pellets and GI motility via the solid-glass bead test. Intestinal barrier integrity was evaluated by means of Ussing chamber experiments (transepithelial electrical resistance (TEER) and 4kDa FITC-dextran passage), complemented by qPCR and immunohistochemistry (IHC) for tight junction proteins (claudin1, ZO1, Occludin and E-cadherin). In a second experiment, chronic intestinal inflammation was induced in 10 months old SAMP8 and SAMR1 mice by administering 2% dextran sodium sulfate (DSS) in 3 cycles of 6 days, alternated with 8 days of normal drinking water. Two days after the last DSS cycle, GI transit and intestinal barrier function were evaluated. Furthermore, several clinical parameters (disease activity index, body weight and colon length), myeloperoxidase activity (MPO; a proxy for neutrophil influx), histopathological scores and the expression of inflammatory transcripts were measured to assess the degree of intestinal inflammation.
Results: At baseline, no significant difference was observed in the GI transit, motility or permeability between SAMP8 and SAMR1 mice, aged 2, 5 and 9 months. In line with Ussing chamber measurements, mRNA and protein abundance of tight junction proteins were similar in both mouse models. However, MPO activity was significantly increased in SAMP8 mice and several pro-inflammatory marker genes were upregulated (Ccl2, Ccl5, Cxcl1, Cxcl10, Ifnα, Il1β, Saa3). We next asked whether a chronic DSS treatment would exacerbate this pro-inflammatory state. While colitis was confirmed by clinical parameters and increased faecal water content in both mice strains, other parameters such as epithelial barrier

function and MPO activity were unaltered. Although DSS treatment induced a subset of pro-inflammatory genes in SAMR1 mice (Ccl3, Cxcl2, Ifnα, Il1β, Il6, Saa3), fewer changes were observed in SAMP8 mice (only Il6).
Conclusions: While no differences in GI parameters were observed between SAMP8 and SAMR1 mice at baseline conditions, we found a significantly higher level of MPO activity and cytokine gene expression in SAMP8, which suggests that there is a pro-inflammatory environment in the gut of 10-month-old SAMP8 mice compared to SAMR1.

- B04 -

DISC1 DISRUPTION ALTERS GASTROINTESTINAL HOMEOSTASIS AND ENTERIC NERVOUS SYSTEM COMPOSITION. K. Tasnády (1), A. Cardilli (2), N. Vaes (1), I. Hamad (2), M. Gijbels (3), M. Kleinewietfeld (2), A. Sawa (4), B. Brône (1), V. Melotte (3), W. Boesmans (1) / [1] Hasselt University, Hasselt, Belgium, Biomedical Research Institute (BIOMED), [2] Hasselt University, Hasselt, Belgium, VIB Laboratory of Translational Immunomodulation, Center for Inflammation Research (IRC), [3] Maastricht University Medical Centre, Maastricht, The Netherlands, Department of Pathology, GROW–School for Oncology and Reproduction, [4] Johns Hopkins University School of Medicine, Baltimore, MD, United States, Department of Psychiatry.

Introduction: Neurodevelopmental disorders such as schizophrenia and autism spectrum disorder often go hand in hand with gastrointestinal (GI) dysfunction. However, the mechanisms underlying GI symptom generation in these diseases that primarily strike the central nervous system remain obscure. Aberrant expression of Disrupted in Schizophrenia 1 (DISC1), a hub and scaffold protein that plays an essential role in neural maturation and connectivity, is an important risk factor associated with the onset of major mental illnesses.
Aim: We aim to understand whether perturbation of DISC1 affects GI homeostasis and enteric nervous system (ENS) function.
Methods: To investigate the effects of DISC1 disruption on the GI tract, we combined mRNA and protein expression studies with standard histology, in vivo assays for gut function and performed microbiota analysis using 16S ribosomal RNA gene amplicon sequencing on adult DISC1 locus impaired (LI) and wild type (WT) littermates.
Results: We first confirmed knockdown of DISC1 in the gut of DISC1 LI mice using qPCR. Whole gut transit time measurements (oral gavage of 6% carmine red) revealed that DISC1 LI mice present with significantly faster GI transit (97.63±27.42 min) as compared to WT littermates (152.8±55.32 min, P=0.0347). While mutant mice also showed a reduced wet weight per stool (6.15±1.95 mg) compared to WT littermates (11.56±4.25 mg, P=0.0086), no changes were observed in stool water content or intestinal permeability (oral gavage of 0.6 mg/g body weight FITC-Dextran). Histopathological alterations (examined using haematoxylin and eosin stainings) were excluded as underlying factor causing altered gut function. This was confirmed by the lack of effect on intestinal inflammatory cytokine (TNF-α, IL-1β, and IL-6) mRNA levels in both the small intestine (SI) and colon (Co). Using immunofluorescence labelling for HuC/D we found that DISC1 LI mice have a higher number of myenteric neurons compared to WT littermates (PSI=0.0939, PCo=0.0101). This is accompanied with reduced gene expression levels of markers for both excitatory (ChAT, PSI=0.0519, PCo=0.0087) and inhibitory (nNOS, PSI=0.0087, PCo=0.5887) enteric neurons. Linear discriminant analysis scoring of colonic microbial content revealed an enrichment of Bacteroides ($P<0.05$), and reduced levels of Muribaculaceae ($P<0.05$) and Clostridia ($P<0.05$) in adult DISC1 LI mice.
Conclusions: We demonstrate that disruption of DISC1 alters GI motility, without inducing intestinal mucosal dysfunction or global changes in intestinal histology. DISC1 LI mice present with increased myenteric neuron numbers and decreased mRNA levels of major enteric neuron subtype markers. Importantly, changes in ENS composition coincide with an imbalance in intestinal microbiota. While speculating an important role for DISC1 in ENS development, our current studies focus on identifying the cellular source(s) of DISC1 in the adult gut and aim to unravel how altered host-microbiota interactions in DISC1 mutant animals contribute to changes in gut function.

- B05 -

AMYLOIDS ACTIVATE NLRP3 IN NEUROSPHERE-DERIVED ENTERIC GLIA, BUT NOT IN ENTERIC NEURONS. N. De Loose (1), P. Verstraelen (1), S. Van Remoortel (1), R. Verboven (1), S. Ibiza-Martinez (1), J. Timmermans (2), W. De Vos (2) / [1] University of Antwerp, Antwerp, Belgium, Laboratory of Cell Biology and Histology, [2] University of Antwerp, Antwerp, Belgium, Laboratory of Cell Biology and Histology; Antwerp Centre for Advanced Microscopy; μNEURO research excellence consortium.

Introduction: Growing evidence suggests a role of the gut-brain axis in amyloid-associated neurodegeneration. Yet, the exact mechanisms remain poorly understood. In the brain, it is well established that chronic inflammation plays a crucial role in the pathogenesis of Alzheimer's disease (AD). The NLRP3 inflammasome, a key molecular link in this neuroinflammatory pathway, has even been implied as a potential target for AD treatment. Given that pathological hallmarks are being phenocopied in the enteric nervous system (ENS), and with the resident microbiome acting as a major source of amyloid-like proteins, we asked whether the NLRP3 inflammasome also becomes activated in the ENS upon amyloid stimulation.

Aim: To characterize the NLRP3 pathway in neurosphere-derived enteric glial and neuronal cultures to amyloids of human and bacterial origin.
Methods: Enteric neurospheres were grown from whole intestine, isolated from E14 embryos, and differentiated after one week towards an enteric glial culture or an enteric neuronal culture using distinct supplemented media. Expression of Toll-like receptors (TLR), TLR-associated genes and the sensor molecule NLRP3 were validated using qPCR. Both cultures were incubated for 24h with bacterial-derived amyloid aggregates (Curli), human amyloid oligomers (Aβ1-42), or peptides with a scrambled sequence (Aβscr). As positive control for NLRP3 activation, the enteric cultures were stimulated with lipopolysaccharide (LPS) and nigericin. After stimulation, medium was collected, and cells were lysed. Cytokine release into the medium was quantified with Meso Scale Discovery (MSD) ELISA. NLRP3 inflammasome activation was assessed by measuring the cleavage of caspase-1 and the release of IL-1β, using respectively western blotting and a IL-1β/IL-1F2 DuoSet ELISA.
Results: We found that tlr1, tlr2, tlr4, tlr9, CD14 and MyD88 were present in both neuronal and glial cultures. Amyloid stimulation resulted in a cell-specific transcriptional alteration of these six genes, which was more pronounced in glial cultures. The NLRP3 sensor molecule was also expressed at baseline but priming with LPS only induced its transcriptional upregulation in glial cultures. Accompanying benchmark experiments in bone marrow-derived macrophages revealed that exposure to LPS and nigericin resulted in a significantly higher release of IL-1β in the medium and the cleavage of caspase-1, both indicative of inflammasome activation. These molecular features were also observed in LPS/nigericin-stimulated neurosphere-derived enteric glial cultures. Stimulation with human Aβ1-42 did not activate the NLRP3 inflammasome after challenging enteric glial cells, but stimulation with Curli was potent enough to bypass priming with LPS. Neither LPS/Nigericin or Aβ1-42 and Curli were capable to induce NLRP3 inflammasome activation in neurosphere-derived enteric neuronal cultures.
Conclusions: We have shown that the TLR machinery is present in neurosphere-derived enteric cultures and that a NLRP3-mediated immune response is induced in a cell-type specific manner. We confirmed that glial cultures react to Curli stimulation via the NLRP3 pathway, whereas enteric neurons do not.

- B06 -

DEVELOPMENT AND MAINTENANCE OF THE ENTERIC NERVOUS SYSTEM ORCHESTRATED BY DEDICATED RESIDENT MACROPHAGES. M. Viola (1), M. Chavero Pieres (1), E. Modave (1), N. Stakenborg (1), M. Delfini (1), T. Martens (2), K. Vandereyken (3), P. Petry (4), A. Sifrim (5), K. Kierdorf (4), M. Prinz (4), P. Vanden Berghe (2), T. Voet (3), G. Boeckxstaens (1) / [1] KUL - University of Leuven, Leuven, Belgium, Center for Neuro-immune Interaction, Translational Research Center for Gastrointestinal Disorders (TARGID), [2] KUL - University of Leuven, Leuven, Belgium, Laboratory for Enteric Neuroscience, Translational Research Center for Gastrointestinal Disorders (TARGID), [3] KUL - University of Leuven, Leuven, Belgium, Department of Genetics, Laboratory of Reproductive Genomics, [4] University of Freiburg, Freiburg, Germany, Institute of Neuropathology, Faculty of Medicine, [5] KUL - University of Leuven, Leuven, Belgium, Laboratory of Multi-Omic Integrative Bioinformatics (LMIB), Department of Genetics.

Introduction: Correct development and maturation of the enteric nervous system (ENS) is critical for survival as it coordinates gut motility, nutrient absorption, and intestinal secretion. At birth, the ENS is immature and requires significant refinement in order to exert its functions in adulthood. However, the mechanisms involved in ENS maturation have not been described. Macrophages are heterogeneous cells that adapt their function according to the needs of the niche in which they reside. Muscularis macrophages (MMØ) are located in close proximity to enteric neurons in the myenteric plexus during adulthood and are critical for neuronal function and survival in adulthood.
Aim: Here, we investigated the functional adaptation of MMØ to evolving tissue requirements, from early postnatal development until after weaning. Furthermore, we investigate their role in the refinement of the ENS early in life, and the role of the ENS in the establishment of a neuro-supportive MMØ phenotype in adulthood.
Methods: Development of the ENS was assessed by immunohistochemical quantification of HuC/D, Neurofilament and Synapsin I at 10, 14, 21 and 56 days after birth. Pruning of synapses and neuronal phagocytosis by MMØ was analysed by quantifying engulfed synapses (Synapsin I+) and engulfed neurons using Imaris and flow cytometry respectively. MMØ were selectively depleted using anti-CSF1R at P10, P21 and 8 weeks and enteric neurons were quantified using immunohistochemistry. Whole-gut intestinal transit using carmine red was used to detect functional consequences of MMØ depletion. Cx3cr1high MMØ were sorted before, and after weaning for scRNAseq via 10X genomics. scRNAseq data was validated via immunohistochemistry and flow cytometry. qRT-PCR was used to detect expression of TGFβ in the muscularis externa and in sorted neurons and enteric glia. Hybridization Chain Reaction (HCR) was used to detect TGFβ transcripts in enteric neurons and glia. Bone-marrow derived macrophages (BMDMs) were cultured for 7 days in the presence of CSF-1 and then stimulated for 24 hours with TGFβ prior to collection of cells for flow cytometry. Enteric denervation was performed in laparotomy using 0.1% benzalkonium chloride (BAC), and tissue was collected after 5 and 14 days for RNA extraction and flow cytometry. A neurotropic AAV9-Cre-GFP viral vector was used to infect TGFb2-3fl mice and flow cytometry was used to assess MMØ populations. Cx3cr1creERT2/WT TGFbr2fl/fl mice were treated with tamoxifen and flow cytometry was used to assess MMØ populations.

Results: The enteric nervous system undergoes refinement during development, with a reduction in neuronal and synaptic density from development to adulthood. This refinement is orchestrated by MMØ, that prune synapses and phagocytose neurons during early postnatal development. Depletion of MMØ caused a significant loss of neurons in adulthood but a significant increase before weaning, accompanied by accelerated intestinal transit. scRNAseq revealed age-specific heterogeneity, with an increase in proliferating MMØ and Lyve1+ before weaning. After weaning, MMØ were predominantly undergoing terminal differentiation, or had acquired a transcriptional profile reminiscent to that of microglia (Tmem119, Hexb, Olfml3) and were closely associated to neuronal cell bodies and neuronal filaments in the muscularis externa (NA-MMØ). NA-MMØ phenotype was induced by TGFβ, which increases after weaning and is produced by the ENS. In line, enteric denervation with BAC led to a reduction in TGFβ3 expression, and the loss of NA-MMØ in the muscularis externa; similarly, AAV9-mediated depletion of TGFβ in the ENS led to loss of MMØ in the muscularis externa. ENS-derived TGFβ signaling required TGFBR2 expression in MMØ, and loss of TGFBR2 expression in MMØ led to loss of NA-MMØ.
Conclusions: We identify a novel role of MMØ in refining the ENS during early postnatal development, via engulfment of synapses and enteric neurons. In adulthood, MMØ are critical for the survival of enteric neurons and adopt a neuron-associated phenotype, which is imprinted by TGFβ produced by the ENS itself. These findings demonstrate the plasticity of MMØ to adapt their function according to the environmental and developmental needs and illustrate their crucial role in ENS maintenance.

- B07 -

BITTER SUBSTANCES IN THE GUT AFFECT THE EXPRESSION OF GROWTH DIFFERENTIATION FACTOR 15 IN PATIENTS WITH OBESITY. Q. Wang (1), M. Farhadipour (1), H. Leng (1), T. Thijs (1), L. Nys (1), L.J. Ceulemans (2), B. Van der Schueren (3), E. Deleus (4), M. Lannoo (5), I. Depoortere (1) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Gut Peptide Research Lab, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Leuven Intestinal Failure and Transplantation (LIFT) Center, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Clinical and Experimental Endocrinology, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Clinical and Experimental Endocrinology, Department of Abdominal Surgery, [5] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Abdominal Surgery.

Introduction: Growth differentiation factor 15 (GDF15), a stress-related cytokine, has recently emerged as a novel satiety factor. It acts via the GFRAL receptor located in the area postrema, the chemoreceptor trigger zone monitoring bitter tasting substances. Bitter taste receptors (TAS2R, 25 subtypes) located on enteroendocrine cells induce the release of satiety hormones and are an important target to reduce appetite. It is currently not known whether bitter substances induce a cellular stress response in the gut to affect GDF15 expression and hence satiety.
Aim: This study aimed to investigate whether bitter substances act via TAS2Rs in gut epithelial cells to increase the expression of GDF15.
Methods: Gastric and proximal small intestinal mucosa were collected from normal weight multi-organ donors (BMI: 24.3±0.5 kg/m2) and patients with obesity (BMI: 41.7±0.7 kg/m2) undergoing Roux-en-Y gastric bypass surgery, respectively. GDF15 expression was confirmed by RT-qPCR and immunofluorescence staining in human gut mucosal tissue sections. Co-staining of GDF15 with epithelial cell markers was performed. Primary crypts isolated from the jejunum of patients with obesity were cultured for 24h and treated with vehicle or bitter substances [gallic acid (GA), azithromycin (AZI), 1,10-phenanthroline (PHE), erythromycin A (EM), diclofenac (DIC), acetaminophen (ACE) or berberine (BERB)] for 4h. The effect of GA and AZI was tested in combination with a TAS2R antagonist, GIV-3727. The effect on the mRNA expression of GDF15 was demonstrated by RT-qPCR.
Results: Relative GDF15 mRNA expression was 77-fold ($P<0.001$) higher in the jejunum from patients with obesity compared to normal weight individuals. Of the GDF15 immunoreactive cells, 50 ± 5% co-localized with the goblet marker mucin 2 and 94 ± 3% with the enteroendocrine cell marker chromogranin A in jejunal tissue sections from normal weight individuals. However, no GDF15-containing cells co-stained with the Paneth cell marker, alpha-defensin 6. The TAS2R4 agonists, gallic acid (0.01-1 mM) and azithromycin (0.075-1 mM) markedly increased GDF15 mRNA expression in a concentration-dependent manner ($P<0.001$) in primary jejunal crypts from patients with obesity. PHE (TAS2R5; 0.1mM), EM (TAS2R10, 1 mM), and BERB (TAS2R46, 0.1mM) increased GDF15 mRNA expression 1.75-fold ($P<0.001$), 4.08-fold ($P<0.001$), and 1.63-fold ($P<0.001$), respectively. The TAS2R14 agonist, DIC (0.15mM) did not affect GDF15 mRNA expression. ACE (TAS2R39, 3mM) decreased GDF15 mRNA expression 0.66-fold ($P<0.05$). The effect of the TAS2R4 agonist, gallic acid, was blocked ($P<0.001$) with the TAS2R4 antagonist GIV-3727. Bitter agonist-induced GDF15 expression correlated with the expression of ATF4 ($P<0.01$) and DDIT3 ($P<0.01$), downstream targets of the unfolded protein response pathway.
Conclusions: GDF15 is more expressed in the jejunum of patients with obesity compared with normal weight individuals. It is present in enteroendocrine and goblet cells. Bitter agonists targeting specific TAS2Rs either increase (TAS2R4, -5, -10, and -46) or decrease (TAS2R39) GDF15 mRNA expression in the gut of obese patients. These bitter agonists may represent an interesting target to affect satiety signaling independent from the hypothalamus.

- B08 -

MAGNETIC RESONANCE IMAGING AS A NON-INVASIVE TOOL TO ASSESS GASTRIC EMPTYING IN MICE.
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Introduction: Methods to study gastric emptying in rodents are time consuming or terminal, preventing repetitive assessment in the same animal. Magnetic resonance imaging (MRI) is a non-invasive technique increasingly used to investigate gastrointestinal function devoid of these shortcomings. Based on our data, we propose MRI as a robust, time-effective and reproducible tool for the non-invasive evaluation of gastric emptying in rodents.
Aim: We evaluated MRI to measure gastric emptying in control animals and in two different models of gastroparesis.
Methods: Mice were scanned using a 9.4 Tesla MR scanner and gastric volume was measured by delineating the areas in which the stomach lumen was observed. Control mice were scanned every 30 min after ingestion of a 0.2 g meal and stomach volume was quantified. The ability of MRI to detect delayed gastric emptying was evaluated in a model of morphine-induced gastroparesis (5mg/kg, sc) and compared to the standard [13C] octanoic acid breath test. Next, MRI was used to detect delayed gastric emptying in a model of streptozotocin-induced diabetes.
Results: Magnetic resonance imaging detected increased gastric volume following ingestion of a standard meal and progressively decreased with a half emptying time of 59 ± 5 min. Reproducibility of the technique was demonstrated by two separate scans at the timepoints of t=60min and t=120min in the same animal, showing comparable volumes (23±1 mm3 scan 1 at t=60 versus 23±2 mm3 scan 2 at t=60; n=5 ; p=0.859 and 21±1 mm3 scan 1 at t=120 versus 21±2 mm3 scan 2 at t=120; n=4 ; p=0.609). Morphine significantly increased gastric volume measured at t = 120 min (saline: 20 ± 2 vs morphine: 34 ± 5 mm3; n = 8–10; $p < 0.001$) and increased half emptying time using the breath test (saline: 85 ± 22 vs morphine: 161 ± 46 min; n = 10; $p < 0.001$). In diabetic mice, gastric volume assessed by MRI at t = 60 min (control: 23 ± 2 mm3; n = 14 vs diabetic: 26 ± 5 mm3; n = 18; p = 0.014) but not at t = 120 min (control: 21 ± 3 mm3; n = 13 vs diabetic: 18 ± 5 mm3; n = 18; p = 0.115) was significantly increased compared to nondiabetic mice.
Conclusions: Our data indicate that MRI is a reliable and reproducible tool to assess gastric emptying in mice and may represent a useful technique to study gastroparesis in disease models or for evaluation of pharmacological compounds.

- B09 -

GENERATION OF HPSC-DERIVED ENTERIC NERVOUS SYSTEM CULTURES FOR FUNCTIONAL IMAGING EXPERIMENTS.
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Introduction: Proper functions of our gut rely on a correctly organized enteric nervous system (ENS). The ENS is the largest and most complicated division of our peripheral nervous system. It comprises numerous neurons and glia that work in a highly-coordinated manner. As the interest in the ENS and its role in neurodegeneration is rapidly rising, new tools are required to model the human-specific situation. Human Pluripotent Stem Cell (hPSC)-derived cultures have become a valuable model to study various cell types and their development as well as to screen drugs for specific diseases. Even though there are differentiation protocols published to generate ENS-like cells, the appearance of these cultures may vary substantially and are not necessarily suitable for all types of experiments. Furthermore, whether hPSC-derived ENS cultures are function-wise comparable to the in situ ENS still remains largely unexplored. Functional assessments for hPSC-derived ENS cultures are so far very scarce, mainly due to a number of practical limitations. For instance, hPSC-derived cells prefer to grow in dense, highly packed and often sphere-like structures. However, these cultures are not suitable for functional measurements, as sufficient resolution to characterize single cells or single organelles cannot be achieved.
Aim: Therefore, we aimed at optimizing the hPSC-derived ENS cultures to better suit optical imaging setups and allow cellular or subcellular functional measurements.
Methods: To this end, published differentiation protocols were modified while monitoring how cells were growing, especially concerning cell density, morphology and 3D appearance. First, during hPSC-differentiation, we introduced an extra dissociation step to split clumping hPSC-derived ENS spheroids as much as possible into single cells. Secondly, we established a scoring system to evaluate the enteric neuron potential of a culture at specific differentiation days based on morphology. Next, we also standardized the protocols and the differentiation timing to facilitate optical activity measurements.
Results: In the optimized cultures, we recorded electrically-induced calcium spikes in neurons, as well as neurotransmitter induced changes using the calcium indicator Fluo4. We measured axonal transport of mitochondria with MitoTracker and confirmed the incidence of synaptic transmission with FM1-43 and post-hoc immunostaining for vAChT. Lastly, with electrophysiological recordings, voltage-dependent currents or current-dependent action potentials could be invoked in these cells.

Conclusions: In summary, with the optimization of established protocols, we are now able to assess functional aspects of single hPSC-derived ENS cells in cultured networks using optical imaging. This approach paves the way to comparing ENS neuronal activity in hPSC-derived cultures with patient-specific mutations (support by CONNECT, FETPROACT-2018-01, GA No 824070, Horizon2020).

- B10 -

IL-22-ACTIVATED JAK1/STAT3-INDUCED MUC13 OVEREXPRESSION COULD AFFECT INTESTINAL MUCOSAL BARRIER FUNCTION THROUGH THE SNAI1/ZEB1 AND ROCK2/MAPK SIGNALLING AXES. W. Arras (1), T. Breugelmans (1), B. Oosterlinck (1), A. Jauregui Amezaga (2), M. Somers (2), B. Cuypers (3), K. Laukens (3), J. G. De Man (1), H. U. De Schepper (2), B. Y. De Winter (4), A. Smet (1) / [1] University of Antwerp, Antwerp, Belgium, Laboratory of experimental medicine and pediatrics, [2] University hospital of Antwerp, Edegem, Belgium, Gastroenterology and Hepatology, [3] University of Antwerp, Antwerp, Belgium, ADReM Data Lab, [4] University of Antwerp/Antwerp University Hospital, Edegem, Belgium, Laboratory of experimental medicine and paediatrics.

Introduction: The transmembrane MUC13 mucin is highly overexpressed in the inflamed colon of inflammatory bowel disease (IBD) patients. Although this mucin is essential to maintain mucosal barrier homeostasis, constitutive overexpression of MUC13 could impact barrier function.
Aim: This study aimed to explore how inflammation-induced MUC13 disrupts epithelial barrier integrity by affecting junctional protein expression in IBD. As a strong correlation between aberrant MUC1 and MUC13 expression has been described in IBD, the involvement of MUC1 was also considered.
Methods: MUC1 and MUC13 siRNA silencing in LS513 cells was performed to explore which upstream and downstream regulators are involved in MUC13-mediated barrier dysfunction upon IL22 stimulation using RNA sequencing and permeability assays. Muc13-/- mice were challenged with dextran sodium sulphate (DSS) to assess acute and chronic colitis, intestinal permeability and the Muc13-related signalling pathways affecting barrier function. Finally, MUC13 expression and its barrier mediators were studied in IBD and control patients.
Results: MUC1 and MUC13 knockdown in intestinal epithelial cells affected gene expression of several barrier mediators in the presence/absence of inflammation. IL-22-induced MUC13 expression impacted barrier function by modulating the JAK1/STAT3, SNAI1/ZEB1 and ROCK2/MAPK signalling pathways, with a cooperating role for MUC1. In response to DSS, opposing effects on disease activity were noticed. More specifically, Muc13 was protective during the acute phase whereas it caused more harm upon chronic colitis. The pathways accounting for the MUC13-mediated barrier dysfunction were also altered upon inflammation in IBD patients.
Conclusions: These novel findings indicate an active role for aberrant MUC13 signalling inducing intestinal barrier dysfunction upon inflammation with MUC1 as collaborating partner.

- B11 -

METABOLIC BALANCE STUDIES IN SHORT BOWEL SYNDROME: TRANSFERABILITY OF FECAL WET WEIGHT AND ENERGY CONTENT MEASUREMENT. A. Verbiest (1), M. Hvistendahl (2), F. Bolognani (3), C. Li (3), O. Khwaja (3), F. Joly (4), T. Vanuytsel (1), P. Jeppesen (2) / [1] KU Leuven - 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 AG, Basel, Switzerland, Clinical Development, [4] Hôpital Beaujon, Clichy, France, Centre for Intestinal Failure, Department of Gastroenterology and Nutritional Support.

Introduction: Short bowel syndrome (SBS) is a rare gastrointestinal condition defined as less than 200 cm of remaining small intestine. Metabolic balance studies (MBS) are the gold standard method to assess intestinal absorptive function in patients with SBS and have had an important role in supporting the mechanistic rationale for new treatment options. However, they are only performed by a few centers around the world. The transferability of MBS is challenging due to the required experience and advanced analysis techniques.
Aim: This study explores the transferability of MBS in patients with SBS to new clinical centers.
Methods: MBS were performed as part of an interventional phase 2 study in Copenhagen (CPH), Leuven (LVN), and Paris. During each MBS, duplicates of meals and drinks, stools, and urine were collected over a 72-hr period. Urine was aliquoted; meals and drinks, and stools were homogenized. MBS samples were stored at -80°C and shipped to the central lab in CPH for freeze drying and full analysis. A collaboration between CPH and LVN (a center without previous MBS experience) was initiated to transfer knowledge on MBS sample processing and analysis. Intensive training sessions were organized by the CPH team, both remotely and on-site. Duplicates of homogenized MBS samples were stored in the LVN lab to analyze the transferability of the quantification of dry matter and energy contents. All samples were freeze-dried, each site using its own equipment, and the dry matter (in g/day) was determined by comparing the weight of the powder versus the initial wet weight of the sample. Energy content was measured in the site-specific freeze-dried powder (C6000

bomb calorimeter, IKA, Germany). Bland-Altman analyses were used to evaluate the bias between results obtained at both sites.
Results: A total of 102 homogenized MBS samples collected from seven patients with SBS from LVN were included in this analysis. The samples were equally distributed among meals and drinks, and stools. When comparing LVN vs. CPH results, the bias for both dry matter and energy content was small, and the overall relative difference was 0.4% and -5.3%, respectively. In addition, Bland-Altman plots showed consistent variability across the graphs.
Conclusions: Our data indicate an excellent reproducibility of dry matter and energy content measurements in a site without previous exposure to MBS after an intensive training program. The favorable results of this analysis provide important insights in the feasibility of MBS transferability in a multi-center setting and opens opportunities for multi-center MBS or the use of MBS in clinical practice to further advance the care and monitoring of patients with SBS. Future prospects include the validation of nitrogen, carbohydrate, lipid and electrolyte measurements across sites as part of full MBS analysis.

- B12 -

MANOMETRIC DIAGNOSIS AND TREATMENT OF RETROGRADE CRICOPHARYNGEAL DYSFUNCTION (R-CPD) F. Vulsteke (1), K. Raymenants (2), S. Arnaert (3), J. Everaert (3), F. Baert (3), T. Vanuytsel (2), J. Tack (2), K. Delsupehe (4), J. Arts (1) / [1] AZ Sint-Lucas Brugge, Assebroek/ Brugge, Belgium, Gastroenterology and Hepatology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [3] AZ Delta, Roeselare, Belgium, Gastroenterology and Hepatology, [4] AZ Delta, Roeselare, Belgium, Otolaryngology, Head and Neck Surgery.

Introduction: Retrograde cricopharyngeal dysfunction (R-CPD), also called 'inability to belch' is a newly recognized disorder characterized by a self-reported inability to belch, accompanied by other gastrointestinal symptoms such as chest/abdominal pain, gurgling noises, bloating and flatulence. It has been linked to an ineffective relaxation of the upper esophageal sphincter (UES) in response to gastroesophageal gas reflux, and botulinum toxin (botox) injection into the UES has demonstrated high success rates in case series (Bastian, 2019). However, in the absence of adequate testing, the diagnosis is often missed. Recently, high resolution impedance manometry (HRiM) with belch provocation test showed promise as a diagnostic tool for these patients (Oude Nijhuis, 2022).
Aim: 1) To confirm manometric findings in patients with R-CPD before and after botox injection, and to compare with HRiM in control patients. 2) To propose a diagnostic and management algorithm for patients with suggestive symptoms.
Methods: We performed a retrospective analysis of HRiM in patients with suggestive symptoms and control patients undergoing the same protocol between May 2021 and November 2022. Ten swallows and a rapid drinking challenge with sparkling water (200 mL or until symptoms were provoked) were added to the Chicago IV protocol, followed by an observation period. Control patients were referred for HRiM for different symptoms or conditions. In patients who underwent botox injection, HRiM was repeated 1 to 5 months later. Gastroesophageal gas reflux was defined as a rapid increase of impedance (>3000Ω) from distal to proximal channels, air entrapment as a period of high impedance levels (>3000Ω) in at least 2 proximal channels (in seconds, divided by the total recording time in minutes), and oscillations as a continuous up and down movement of air.
Results: HRiM with belch provocation test was available for 19 patients before, and 5 patients after botox injection. Typical symptoms were present in all patients. Normal UES relaxation occurred after deglutition in all patients. Mean observation period after drinking challenge with sparkling water was 7.8 minutes. We observed a mean of 2 gastroesophageal gas reflux events per minute, which resulted in UES relaxation in only 6% of events. Air entrapment occurred in 22 sec/min, and oscillations in 28 sec/min. After botox injection, 4/5 patients improved. 3/5 patients were able to belch during the observation period, and the mean air entrapment time was reduced to 8 sec/min. In control patients (n=18), a drinking challenge with sparkling water induced gastroesophageal gas reflux with adequate belching in all patients, with air entrapment or oscillations in 9 sec/min.
Conclusions: We can confirm typical findings on HRiM with belch provocation test, which are not present in control patients. Liquid swallows with sparkling water were unable to differentiate R-CPD patients from controls, however a drinking challenge with sparkling water provoked symptoms and typical manometric anomalies in patients, but not controls. Botox injection reverses the abnormalities on HRiM. These findings can provide a basis for a diagnostic algorithm and a standardized HRiM protocol for patients presenting with 'inability to belch'.

- B13 -

COMPARISON OF THE PREVALENCE AND IMPACT OF DISORDERS OF GUT-BRAIN INTERACTION IN THE FRENCH- AND DUTCH-SPEAKING POPULATIONS IN BELGIUM. E. Devolder (1), B. Broeders (1), M. Jones (2), M. Simren (3), S. Bangdiwala (4), A. Sperber (5), O. Palsson (6), J. Tack (1) / [1] KU Leuven - University of Leuven, Leuven, Belgium, Gastroenterology, [2] University of New South Wales, Sydney, Australia, Gastroenterology, [3] university of Göteborg, Göteborg, Sweden, Neurogastroenterology, [4] University of North Carolina at Chapel Hill, ,

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Introduction: Disorders of Gut-Brain Interaction (DGBI), formerly called functional gastrointestinal disorders are highly prevalent and impact on psychosocial well-being, quality of life and healthcare utilization. The Rome Foundation carried out a worldwide epidemiology study on DGBI according to the Rome IV criteria in 33 countries, including Belgium. The Belgian survey was conducted through the internet and comprised 2021 respondents' representatives for the adult population, including the proportion of French- and Dutch-speaking persons and their geographical distribution.
Aim: We analysed the prevalence rates of all 22 DGBI and their impact in Belgium and in the two language groups.
Methods: The survey included demographics and questionnaires to assess Rome IV diagnostic categories, quality of life, anxiety, depression, somatization, healthcare utilization and concern about digestive problems.
Results: 2021 participants completed the survey in Belgium. In total, 38.5% met diagnostic criteria for at least one DGBI. The disorders with the highest overall prevalence were functional constipation (11.7%, [10.3-13.2%]), unspecified functional bowel disorder (9.0%, [7.8-10.3%]), Rome III IBS (8.7%, [7.5-10.0%]), and functional dyspepsia (6.2%, [5.2-7.4%]). DGBI prevalence was higher in the French-speaking than in the Dutch-speaking population (43% [39-46%]) vs. 35% [33-38%]). Statistically significant differences in prevalence between the language groups were found for some DGBI, such as functional bloating (respectively 1.8 and 3.6%, p=0,008). The difference was greatest in functional dyspepsia, (4.5% in Dutch-speaking vs. 8.5% in French-speaking patients, p<0,001; respectively for epigastric pain syndrome (EPS) and post prandial distress syndrome (PDS) 1.4% vs. 2.6% and 4.0% vs. 7.3%). There were no significant differences in the prevalence of IBS, functional diarrhea and chronic constipation. Furthermore, having one or more DGBI was negatively associated with psychosocial well-being. The scores for depression were lower in the Dutch-speaking participants with one or more DGBI compared with the French-speaking population (1,63 ± 1.68 vs. 1,39 ± 1,69 p=0.013). Interestingly, we also found significantly lower scores in the general Dutch speaking population for anxiety (1,22 ± 1,52 vs. 0,88 ± 1,32 p<0.001), depression (1,09 ± 1,37 vs. 0,59 ± 1,09 p<0,001), and somatization (4,59 ± 3,26 vs. 4,22 ± 3,14 p=0.046). Dutch-speakers had higher global physical health component score (14,79 ± 2,37 vs. 15,31 ± 2,50 p<0,001) and global mental health component score (14,06 ± 3,02 vs. 14,50 ± 2,96 p=0,006). When having one or more DGBI was controlled for, anxiety and depression scores were lower in Dutch-speaking than French-speaking individuals (respectively OR 0.888, [0.842-0.937]; and OR 0.813, [0.764-0.964]). The use of medications for constipation, diarrhea, nausea, heartburn, pain, gas and bloating, anxiety, depression and sleeping was higher in the group with at least one DGBI (p-value <0.001). In the Dutch-speaking group, the medication use for gastric acid was lower (OR 0.779, [0.615-0.987]), but the use of prescribed analgesics was more common (OR 1.331, [1.051-1.686]). Nevertheless, the use of non-prescribed pain medication was higher in the French-speaking group (OR 0.755, [0.606-0.941]). The use of medication for anxiety and sleep was also higher in the latter group (OR 0.521, [0.387-0.701] and OR 0.697, [0.536-0.907]). There was no difference in the intake of medications for diarrhea, nausea, gas/bloating and depression. We also found no significant difference in doctor visits and impact on daily activities and roles between the Dutch-and French-speaking group.
Conclusions: The results of this study provide the first in-depth assessment of the prevalence of Rome IV DGBI in the Dutch-and French-speaking population in Belgium, showing a higher DGBI burden in the latter group. Further studies will be needed to establish the linguistic, socio-economic, lifestyle or pathophysiological basis of these differences.

- B14 -

DIAGNOSING AND MANAGING IBS IN CLINICAL PRACTICE: ONLINE SURVEY AMONG GASTRO-ENTEROLOGISTS AND GENERAL PRACTITIONERS. P. Casteels (1), H. Reynaert (2), S. Kindt (1) / [1] Vrije Universiteit Brussel (VUB), Jette, Belgium, Gastroenterology, [2] Vrije Universiteit Brussel (VUB), Jette, Belgium, Gastroenterology.

Introduction: Irritable bowel syndrome (IBS) represents the most common disorder of gut-brain interaction encountered in clinical practice. The Rome IV criteria define the disorder. Over the years, many guidelines proposed guidance during the diagnostic and therapeutic approach of patients with presumed IBS.
Aim: This study explores habits in the management of IBS in daily practice and confronts these with the recently published recommendations of the Belgian IBS consensus.
Methods: We conducted an online survey exploring the diagnostic and therapeutic approach of patients suffering from IBS with predominant diarrhea (IBS-D) in primary and secondary care using an online vignette-based survey in Dutch and French between January and July 2022.
Results: Sixty-four gastroenterologists and 31 general practitioners completed the survey. Abdominal pain and abdominal discomfort as cardinal symptom resulted in a diagnosis of IBS by resp. 88% and 84%. Diagnostic workup usually consists of biochemical testing (85%), fecal blood test (48%), stool analysis for Clostridioides and parasites (64%). Only one out of five respondents test for coeliac disease and hyperthyroidism. 18% order breath testing. In the older patient case, 25% plan a colonoscopy with biopsies. Antispasmodics (28%) and dietary interventions (20%) represent the preferred

first-line treatment. In case of refractory symptoms, 58% of general practitioners refer the patient to a specialist. 20% of gastroenterologists start a neuromodulator and 13% initiate bile acid sequestrants in second and third line.
Conclusions: Contrasting with the ROME IV criteria, healthcare practitioners make no distinction between abdominal pain and discomfort when considering a diagnosis of IBS. Most physicians order only limited additional non-invasive testing, as recommended by the guidelines. In contrast to the recommendations, breath testing is frequently ordered. Antispasmodics and dietary interventions represent the preferred first-line treatment options. Management appears highly variable upon failure of initial treatment. Education should target the observed discrepancies with existing recommendations.

- B15 -

DUODENAL EOSINOPHILS AND RELEASE OF EOSINOPHIL-DERIVED PROTEINS ARE LINKED TO SYMPTOMS IN FUNCTIONAL DYSPEPSIA WITH EOSINOPHIL-DECREASING EFFECTS OF HIGH-DOSE PROTON PUMP INHIBITORS. M. Ceulemans (1), P. Huyghe (1), A. Cetin (1), A. van de Geer (1), M. Horiguchi (1), I. Gutiérrez (1), J. Tóth (1), I. Jacobs (1), J. Cremer (2), L. Wauters (1), M. Carlson (3), G. De Hertogh (4), J. Tack (1), T. Vanuytsel (1) / [1] KUL - University of Leuven, Leuven, Belgium, TARGID, [2] KUL - University of Leuven, Leuven, Belgium, Allergy and Clinical Immunology, [3] Uppsala university, Sweden, Gastroenterology Research Group, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Pathology.

Introduction: Duodenal eosinophil infiltration and degranulation have been reported in functional dyspepsia (FD) but no detailed study of innate leukocytes apart from routine histology has been performed (Ceulemans et al. Frontiers Neuroscience 2022). In addition, the potential of eosinophilic proteins, including eosinophil-derived neurotoxin (EDN), as diagnostic markers in FD remains unclear. Eosinophil-reducing effects of proton pump inhibitors (PPI) were demonstrated in FD by cell counts on histology (Wauters et al. Gastroenterology 2021). Moreover, high-dose PPI therapy is routinely used as anti-inflammatory therapy in eosinophilic esophagitis, but the effect of high-dose PPI remains unknown in FD.
Aim: We aimed to perform a detailed assessment of innate cell populations in the duodenum via flow cytometry to evaluate their role in FD and check the concordance of flow cytometry with routine histological evaluation. Furthermore, we aimed to evaluate the potential anti-inflammatory effects of a high-dose PPI-course in FD.
Methods: FD patients (Rome IV) and healthy controls (HC) underwent upper GI endoscopy with duodenal biopsies, repeated in FD on-PPI (pantoprazole 40mg bid, 4 weeks). GI symptoms were scored using the PAGI-SYM questionnaire. Duodenal lamina propria cells were isolated, stained and acquired on an LSR Fortessa flow cytometer (BD). Single viable cells were gated as leukocytes (CD45+) and subsequently eosinophils (Siglec8+, CD117-, CD16-, CD193+, CD123-, SSChigh), mast cells (Siglec8+, CD117+) or neutrophils (CD16+, SSChigh) with additional CD69 staining as activation marker. Eosinophils (H&E staining) and mast cells (cKit/CD117 staining) were counted on scanned biopsy slides in 3 non-overlapping fixed-sized regions (0.264mm²). EDN was measured in duodenal biopsy supernatants and faecal protein extracts from frozen stool samples (Peterson et al. Am J Gastro 2002) using ELISA (Diagnostics Development). Analyses were conducted in Prism with (non-)parametric tests depending on normality and calculation of Spearman's correlation r.
Results: Data were obtained from 18 FD patients (14 female, mean ± SEM age 31 ± 2 years) and 17 HC (14 female, 31 ± 2 years) with flow cytometry data available from 11 FD and 16 HC. Symptoms were significantly higher in FD vs HC (2.1 ± 0.2 vs 0.3 ± 0.1, p<.0001) and decreased in FD on-PPI (1.5 ± 0.3, p=.007). Leukocytes (7.1 ± 1.3% vs 4.2 ± 0.5%, p=.014) and eosinophils (0.2 ± 0.06% vs 0.09 ± 0.02%, p=.034) decreased in FD on-PPI with a similar trend for neutrophils (0.04 ± 0.006% vs 0.03 ± 0.006%, p=.098), without between-group differences. Overall, the majority of eosinophils (98.4 ± 0.2%) and mast cells (98 ± 0.5%) were CD69+ (p=.62), with a significantly lower proportion of CD69+ neutrophils (35.1 ± 3.6%, p< .0001 vs eosinophils and mast cells). There was no effect of FD status on CD69 expression within the eosinophil and mast cell populations, although the proportions of CD69+ eosinophils (2.6 ± 0.5% vs 2.4 ± 0.5%, p=.004) but not mast cells (2.7 ± 0.2% vs 3.3 ± 0.4%, p=.21) decreased on-PPI. Eosinophils on H&E were not different between HC and FD (87 ± 16/mm² vs 85 ± 17/mm², p=.87) or after PPI (74 ± 13/mm², p=.46), nor were histological mast cell counts (HC: 440 ± 39/mm² vs FD: 395 ± 34/mm², p=.39; FD on-PPI: 391 ± 28/mm², p=.36). In FD, histological eosinophil (r=0.46, p=.05) and mast cell (r=0.58, p=.009) counts correlated with their proportions on flow cytometry, respectively, whereas in HC these associations were not significant for eosinophils (r=0.54, p=.18) or mast cells (r=-0.10, p=.57). Supernatant and faecal EDN concentrations were not significantly different between or within groups. In FD, the proportion of eosinophils was linked to supernatant (r=0.58, p=.005) but not faecal EDN (r=-0.02, p=.92), whereas a trend for the opposite was found in HC (faecal EDN: r=0.50, p=.06; supernatant EDN: r=-0.12, p=.67). GI symptoms were linked to eosinophils (r=0.53, p=.02) and supernatant EDN (r=0.42, p=.02) in FD, but not mast cells, neutrophils or faecal EDN.
Conclusions: In FD, duodenal eosinophils and biopsy-derived EDN were linked to GI symptoms, highlighting the relevance of duodenal eosinophils in FD. Using flow cytometry, we confirm anti-inflammatory effects of a high-dose PPI course in FD through decreased duodenal leukocytes, total and activated eosinophils, and partly neutrophils, but not mast cells, although these populations were similar between FD and controls.

- B16 -

STUDY ON THE ROLE OF MRGPRX2-MEDIATED MAST CELL ACTIVATION IN IBS. L. Decraecker (1), M. Cuende-Estévez (1), R. Quan (1), H. Hussein (1), A. Denadai-Souza (1), M. Viola (1), J. Aguilera-Lizarraga (2), N. Stakenborg (1) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing, [2] University of Cambridge, Cambridge, United Kingdom, Department of Pharmacology.

Introduction: Mast cells (MCs) are classically activated by IgE, which in the gut leads to their degranulation and the development of abdominal pain. However, MCs can also be activated in an IgE-independent manner via the binding of basic peptides to MRGPRX2. To what extent MRGPRX2-mediated MC activation is involved in abnormal pain perception in irritable bowel syndrome (IBS) remains unknown.
Aim: Our first aim was to determine whether MRGPRX2 is expressed in MCs in the human colon and rectum. We then investigated the presence of MRGPRX2 agonists in the human gut. To determine whether MRGPRX2 signaling might play a role in IBS, we compared the levels of MRGPRX2 expression on MCs and MRGPRX2 agonists in rectal biopsies from healthy controls and patients with IBS. Finally, we aimed to investigate whether MRPGRX2 agonists can trigger MC degranulation in the colon submucosal plexus.
Methods: Rectal biopsies were collected from IBS patients and healthy volunteers (HV) who were recruited by public advertisement. Healthy colon samples were dissected from resection tissue from individuals undergoing a hemicolectomy. MRGPRX2 expression was measured in healthy human colon by immunofluorescence (IF), in rectal biopsies by qPCR and IF, and by flow cytometry in the colon. Additionally, we evaluated MRGPRX2 agonistic activity of rectal biopsy supernatants from HV and IBS on MRGPRX2-transfected CHO cells and measured the concentration of the MRGPRX2 agonists CORT-17, LL-37, and substance P in rectal biopsy supernatant. The ability of the MRGPRX2 agonist C48/80 (10µg/ml) to degranulate MCs was determined using in situ MC live imaging in human submucosal preparations. All results are presented as mean +/- SD, and groups were compared using One-Way ANOVA with correction for multiple testing, or unpaired t-test, as appropriate.
Results: Using IF, most MCs were identified in the mucosa compared to submucosa and muscularis in both colon ascendens and descendens. Using flow cytometry, we showed that mainly MCs in the submucosa and muscularis express MRGPRX2 (mucosa; 4±4% of MCs, (n=7), submucosa: 26±18% of MCs (n=7), muscularis externa: 25±13% of MCs (n=6), p=0.01). No difference in MRGPRX2 gene expression (HV (n=19): 0.08±0.06 2-ΔCT vs IBS (n=31): 0.10±0.13 2-ΔCT, p>0.05) or IF (HV (n=11): 5.9±12.6% MRGPRX2+ MCs vs IBS (n=22): 11.0±18.2% MRGPRX2+ MCs, p>0.05) was detected between HV and IBS in rectal biopsies. Calcium imaging experiments with MRGPRX2-transfected CHO cells showed that supernatant from both HV and IBS patients contains MRGPRX2 agonistic activity. Of note, 9 of the 21 IBS samples revealed MRGPRX2 activity above the 95th percentile of that of HV samples (n=7). Substance P levels (HV (n=17): 81±62 pg/mg protein vs IBS (n=24):166±99 pg/mg protein, p=0.004) were augmented in IBS supernatant compared to HV, but not CORT-17 or LL-37 levels (HV: n=10, IBS: n=9). Finally, using live imaging, we observed that 10 µg/ml C48/80, but not vehicle, triggers MC degranulation in the human colonic submucosa.
Conclusions: MCs located in the human colon and rectum express MRGPRX2 and are degranulated by activation of this receptor. Our finding that more MRGPRX2 agonistic activity can be detected in biopsies of a subgroup of IBS patients suggests that MRGPRX2-mediated MC degranulation may be an interesting target to treat abdominal pain in IBS.

- B17 -

CONFOCAL LASER ENDOMICROSCOPY FOOD ALLERGY TESTING IN FUNCTIONAL DYSPEPSIA AND IRRITABLE BOWEL SYNDROME. J. Stevenheydens (1), L. Balsiger (1), J. Schol (1), K. Raymenants (1), K. Routhiaux (1), J. Toth (1), F. Carbone (1), T. Vanuytsel (1), J. Tack (1) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Gastroenterology.

Introduction: Functional dyspepsia (FD) and irritable bowel syndrome (IBS) are two of the most common functional gastrointestinal diseases, defined by the Rome IV criteria. FD comprises the subgroups postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS). In FD, increased duodenal eosinophil counts and decreased mucosal integrity have been implicated in symptom generation while in IBS a major role in pathogenesis is attributed to intestinal mast-cells. Food induced symptoms occur in both diseases, possibly mediated through local immune cell activation facilitated by increased mucosal permeability. Confocal laser endomicroscopy (CLE) previously showed acute food-triggered disruption of the duodenal epithelial barrier in IBS.
Aim: The aim of the current study was to evaluate whether in FD and IBS, acute mucosal alterations resulted in increased permeability measures ex vivo and whether alterations in duodenal permeability were present at baseline.
Methods: In Rome IV IBS-D and FD patients, classical allergic sensitization to nutrients was excluded by specific serum IgE tests. CLE was performed during upper GI endoscopy after i.v. 2.5 mL fluorescein 10% administration and duodenal mucosa was visualized before and after sequential application of 10mL dissolved aliquots of fish, nuts, egg white, soy, milk and wheat protein. The procedure was stopped after a positive reaction. Duodenal biopsies were obtained at baseline

and after food exposures to evaluate trans-epithelial electrical resistance (TEER) in mini Ussing chambers. Data are reported as mean±SEM. Results were considered significant if $p<.05$.
Results: In total, 15 patients were recruited. Eight patients suffered from predominantly FD symptoms (100% female, 31±5y, BMI 22.6±0.7kg/m², 4/8 PDS, 1/8 EPS, 3/8 overlap EPS/PDS). Two FD patients also had overlapping IBS. Seven patients suffered from predominantly IBS (100% female, 37±6y, BMI 20.5±1kg/m²,3 IBS-D, 3 IBS-M, 1 IBS-U). Five patients with IBS had overlapping FD. After food exposure, acute positive reaction with extravasation of fluorescein and cell shedding was seen on CLE. In total, 80% of patients exposed to wheat reacted positively, 50% to soy, 40% to milk, 33% to egg, 25% to fish and 22% to nuts. One patient presented a leaky mucosa at baseline rendering interpretation impossible. At baseline, TEER from FD and IBS patients was not different 30.4±2.5 Ω.cm² vs 29.2±1.6 Ω.cm² ($p=0.67$) from healthy controls. Compared to baseline, TEER was numerically lower after food exposure (30.4±2.5 Ωcm² vs.27.4±1.7 Ωcm², $p=0.38$) but no significant change was measured.
Conclusions: In FD, IBS and overlap of both conditions, CLE demonstrates duodenal atypical food-allergy-type reactions. CLE findings of food-triggered disruption of the epithelial barrier did not result in altered measures of permeability ex vivo in this cohort. Compared to healthy volunteers, the ex vivo permeability at baseline was not different. The observed changes in the mucosa seem to reflect acute capillary extravasation rather than acute permeabilization of the mucosa. The underlying mechanism of the observed CLE changes requires further investigation.

- B18 -

INVESTIGATING THE IMMUNE RESPONSE USING SCRNA-SEQ IN IRRITABLE BOWEL SYNDROME. H. Hussein (1), H. Modave (2), M. Delfini (2), G. Boeckxstaens (2) / [1] KUL - University of Leuven, Leuven, Belgium, TARGID, [2] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism (CHROMETA).

Introduction: Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal disorder estimated to affect 5 to 20% of the general population and which seriously impairs quality of life. It is 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. VHS manifests as a painful response to normally innocuous stimuli (allodynia) and/or an exaggerated response to painful stimuli (hyperalgesia). VHS often occurs in IBS patients after eating certain foods. Indeed, up to 84% of patients with IBS report a rapid onset or exacerbation of their GI symptoms following intake of specific foods. An exacerbated mast cell response, due to higher mast cell numbers or increased degranulation, has been proposed to underlie VHS, although until recently the stimuli triggering such a response, particularly in response to food antigens, were unknown. Our most recent work has 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. Preventing IgE-mediated activation of mast cells normalized abdominal pain levels in sensitized mice. In patients with IBS, the injection of food antigens, such as gluten, wheat or soy, into the colonic mucosa induced a local edema. Importantly, those patients did not exhibit allergy to the injected food antigens, suggesting that a local immune response to food antigens also occurs in the gut of those patients and could underlie abdominal pain development. The cellular actors and immune mechanisms underlying the development of a local intestinal immune response against food antigens and their role in abdominal pain development are currently unknown.
Aim: In this study, we aim to characterize the immune mechanisms and cellular actors involved in the development of pain in IBS patients. To do so, we performed single cell transcriptomics on a cohort of healthy and IBS patients. Because the pathophysiological mechanisms leading to IBS development are likely to vary from one subtype to another, we included the three IBS subtypes associated with abnormal stool patterns: IBS with predominant constipation (IBS-C), IBS with predominant diarrhoea (IBS-D) and IBS with a mixed stool pattern (IBS-M).
Methods: Five healthy volunteers who were free of abdominal symptoms, with no history of gastrointestinal disease or previous gastrointestinal surgery were recruited by public advertisement. Nineteen participants with IBS meeting the ROME III criteria were recruited from the outpatient clinic of the University Hospitals Leuven, and further classified into their respective stool subtypes (6 IBS-D, 7 IBS-C and 6 IBS-M). Rectal biopsies from IBS patients or healthy subjects were taken during proctoscopy. Single cell suspensions of rectal biopsies were then obtained by enzymatic digestion following a step of epithelial removal. 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 were integrated at the CD45 level. We then identified immune cell populations and investigated changes in population enrichment or gene expression.
Results: Using classical immune populations markers, we identified cell clusters corresponding to antibody-secreting cells (SDC1), B cells (CD19), T cells (CD3D), NK cells (KLRF1), myeloid cells (CD14), mast cells (KIT, TPSAB1), innate lymphoid cells (KIT, RORC), fibroblasts (COL1A2), epithelial cells (EPCAM), endothelial cells (PECAM1) and proliferating cells (MKI67). An enriched proportion of antibody-secreting cells was found among the IBS group compared to healthy. Upon examining distinct IBS subtypes, we noticed that IBS-D and IBS-C groups show an increased

enrichment of antibody-secreting cells, whereas the IBS-M group showed an increase in B cells and a decrease in T cells. Interestingly, IGHE expressing cells were enriched in IBS compared to healthy, in line with our previous findings.
Conclusions: Our preliminary results support the development of a type 2 immune response as an underlying cause of IBS and abdominal pain development in human patients. This dataset will allow us to thoroughly investigate the immune mechanisms involved in pain IBS development.

- B19 -

RETROGRADE CRICOPHARYNGEUS DYSFUNCTION (R-CPD): SINGLE CENTER CASE SERIES AND TREATMENT RESULTS OF A NEWLY DISCOVERED MOTILITY DISORDER. S. Arnaert (1), J. Arts (2), F. Baert (1), K. Delsupehe (3) / [1] AZ Delta, Roeselare, Belgium, Gastroenterology, [2] AZ Sint-Lucas Brugge, Assebroek/ Brugge, Belgium, Gastroenterology, [3] AZ Delta, Roeselare, Belgium, Otolaryngology, Head and Neck Surgery.

Introduction: Retrograde Cricopharyngeus Dysfunction (R-CPD) is a new clinical entity characterized by inability to belch and associated symptoms of loud gurgling noises, chest and abdominal pressure or abdominal bloating and excessive flatulence.[1,2] It is hypothesized that a dysfunction of the upper oesophageal sphincter (UES) (cricopharyngeus muscle) causes the inability to belch or burp.[1,3] First described by Bastian, R-CPD is a syndrome diagnosed clinically and can be treated with botulinum toxin (BT) injection in the UES. As only 3 case series have been reported, the condition and results of the treatment are poorly understood. We hereby report treatment results of a series of consecutive patients who presented at our center with symptoms of R-CPD/inability to burp.
Aim: To report patient demographics, symptomatology, and short- and long-term postoperative results of R-CPD.
Methods: Data on 43 consecutive patients presenting with R-CPD were prospectively collected using a standardized questionnaire prior to and 1 month after treatment. All patients were diagnosed using the clinical symptoms proposed by Bastian. Long-term results were recently collected. Botulinum toxin injection procedures were performed under general anaesthesia in day surgery.
Results: 43 patients (23F) were included, median age at presentation was 29 years (range 20-65). Median BMI was 22.6 kg/m² (range 16.5-37.5). All patients reported invalidating very similar symptoms for a median of 23 years (in 64.3% since childhood). Inability to belch and gurgling noises were present in all patients, >90% of patients experienced abdominal/chest discomfort, abdominal bloating and social inhibition as a result of their condition. One month after injection of BT, 46.3% of patients experienced complete relief of symptoms, 43.9% good symptom improvement and 9.8% no improvement. At median follow-up of 32 months postoperatively, 47.1% (n=16/34) of patients reported persistent complete relief of symptoms, 11.7% good relief of symptoms (n=4/34), in 20.6% some relief (7/34) and 20.6% loss of or no response (n=7/34). Only side effect was transient swallowing difficulties (n=4).
Conclusions: Our case series confirms the clinical syndrome of R-CPD with excellent short-term and very good long-term relief of symptoms after injection of botulinum toxin. Further research is ongoing to understand the underlying pathophysiology and to evaluate if high resolution impedance manometry (HRIM) with belch provocation test could be a diagnostic tool. References: 1. Bastian RW, Smithson ML. Inability to Belch and Associated Symptoms Due to Retrograde Cricopharyngeus Dysfunction: Diagnosis and Treatment. OTO Open. 2019;3(1). 2. Wajsberg BA, Hoesli R, Wingo M, Richardson B, Bastian RW. Retrograde Cricopharyngeus Dysfunction (R-CPD): An Orphan Disease? American Journal of Gastroenterology 2022 (117) 1539. 3. Karagama Y. Abelchia: inability to belch/burp – a new disorder? Retrograde cricopharyngeal dysfunction (RCPD). Eur Arch Oto-Rhino-Laryngology. 2021;278(12):5087–91.

- B20 -

MUCIN-MICROBIOME SIGNATURES SHAPE THE TUMOUR MICROENVIRONMENT IN GASTRIC CANCER. B. Oosterlinck (1), W. Arras (2), J. De Man (2), K. Geboes (3), H. De Schepper (4), M. Peeters (5), S. Lebeer (6), J. Skieceviciene (7), G. L. Hold (8), J. Kupcinskas (7), A. Link (9), B. Y De Winter (2), A. Smet (2) / [1] University of Antwerp, Antwerp, Belgium, LEMP, [2] University of Antwerp, Antwerp, Belgium, Laboratory of Experimental Medicine and Paediatrics, [3] University Hospital Ghent (UZ Gent), Gent, Belgium, Pathology Department, [4] Antwerp University Hospital, Edegem, Belgium, Division of Gastroenterology and Hepatology, [5] University Hospital Antwerp, Edegem, Belgium, Department of Oncology, [6] University of Antwerp, Antwerp, Belgium, Department of Bioscience Engineering, [7] Lithuanian University of Health Sciences, Kaunas, Lithuania, Department of Gastroenterology and Institute for Digestive Research, [8] University of New South Wales, Sydney, Australia, Microbiome Research Centre, [9] Otto von Guericke University Magdeburg, Magdeburg, Germany, Department of Gastroenterology, Hepatology and Infectious Diseases.

Introduction: One of the hallmark features of gastric adenocarcinomas is aberrant mucin expression, with gastric- and intestinal-type mucins being widely expressed in gastric tumours. The clinical role of mucins in relation to disease progression and outcome is still controversial. Furthermore, the gastric microbiome is also believed to contribute to gastric carcinogenesis. Mucins can act as binding sites or metabolic substrates for bacteria and the abundance of gastric or intestinal-type mucins plays thus an important role in the site-specific colonization of bacteria in the gastric mucosa.

Aim: We aimed to identify mucin-microbiome signatures shaping the tumour microenvironment in gastric adenocarcinomas and predicting clinical outcome.
Methods: We performed high-throughput profiling of the mucin phenotypes present in 108 gastric adenocarcinoma cases and 20 functional dyspepsia controls using validated mucin-based RT-qPCRs with subsequent immunohistochemistry validation and correlated the data with clinical outcome parameters. The gastric microbiota was assessed by 16S rRNA gene sequencing, taxonomy and community composition were determined, microbial networks analysed, and the metagenome inferred in association with mucin phenotypes and expression.
Results: The tumour samples were classified as gastric (predominantly MUC5AC, MUC6 and MUC1; 13%), intestinal (predominantly MUC2, MUC4 and MUC13; 19%), mixed (all types; 47%) and null (neither gastric nor intestinal; 17%) mucin phenotypes. Gastric adenocarcinomas with an intestinal mucin environment or high/low-level MUC13 expression, associated with poor survival ($p= 0.01$, log-rank test). On the contrary, gastric MUC5AC or MUC6 abundance was associated with a more favourable outcome ($p < 0.05$, log-rank test). The oral taxa Neisseria, Solobacterium, Leptotrichia, Prevotella, Veillonella had significant centralities in tumours with MUC13 overexpression highlighting their role as potential drivers in MUC13 signalling in GC. Furthermore, dense bacterial networks were observed in intestinal and mixed mucin phenotype tumours whereas the lowest community complexity was shown in null mucin phenotype tumours due to higher Helicobacter abundance resulting in a more decreased diversity. Significant enrichment of oral or intestinal microbes was mucin phenotype dependent. Although intestinal and null mucin phenotype tumours, showed an overall enrichment of intestinal taxa, they also favoured the establishment of some pro-inflammatory oral taxa forming strong co-occurrence networks.
Conclusions: Our results emphasize key roles for mucins in gastric cancer prognosis and shaping microbial networks in the tumour microenvironment. Specifically, the enriched oral taxa associated with aberrant MUC13 expression can be potential biomarkers in predicting disease outcome.

- B21 -

IMPROVED WET WEIGHT ABSORPTION AFTER 1-MONTH APRAGLUTIDE TREATMENT IN SHORT BOWEL SYNDROME WITH INTESTINAL FAILURE AND COLON-IN-CONTINUITY. A. Verbiest (1), M. Hvistendahl (2), F. Bolognani (3), C. Li (3), O. Khwaja (3), F. Joly (4), P. Jeppesen (2), T. Vanuytsel (1) / [1] KU Leuven - 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 AG, Basel, Switzerland, Clinical Development, [4] Hôpital Beaujon, Clichy, France, Centre for Intestinal Failure, Department of Gastroenterology and Nutritional Support.

Introduction: Short bowel syndrome (SBS) is a rare gastrointestinal condition with a high risk of developing intestinal failure (SBS-IF) with a need for 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 the short-acting GLP-2 analog teduglutide in patients without a remaining colon. However, the impact of GLP-2 analogs on fluid and energy absorption in SBS-IF with a colon-in-continuity (CiC) is unclear. Apraglutide (APRA) is a new, long-acting GLP-2 analog that is in development for SBS-IF.
Aim: We performed a pre-defined interim analysis of a phase 2 study in SBS-IF-CiC to investigate the safety and efficacy of 4-weeks APRA treatment based on metabolic balance studies (MBS).
Methods: STARS Nutrition is a 52-week multicenter, open-label, phase 2 study in adult patients with SBS-IF-CiC receiving weekly subcutaneous APRA injections. 72-hour MBS were performed at baseline and after 4 weeks of treatment and were followed by a 48-week PS adjustment period. During the MBS, oral fluid intake was kept constant by adhering to an individual predefined drinking menu. Duplicates of meals and fluids (wet weight intake) were collected as well as urine and feces (fecal wet weight output). PS was not adjusted in this period. Safety was the primary endpoint. Secondary endpoints included changes in fecal wet weight output, wet weight absorption, urinary output, and energy absorption by bomb calorimetry. Data are presented as mean (95% CI) unless specified otherwise. Nominal p-values are calculated using Wilcoxon matched-pairs signed rank 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. At baseline, patients received a weekly PS volume of 10 (range 4-21) L. Seven patients experienced a total of 23 adverse events (AEs) of which 4 patients experienced 6 treatment-emergent AEs. No AEs were considered notable based on their nature or severity. Fecal wet weight output decreased significantly by 253 (-437 – -68) g/day ($p=0.012$). Relative wet weight absorption increased by 9 (1 – 18) % ($p=0.039$). There was a numeric increase in urinary output, which failed to reach statistical significance ($p=0.129$). For energy absorption, no statistically significant changes were observed.
Conclusions: These initial short-term results of APRA in SBS-IF-CiC support safety and efficacy in increasing fecal wet weight absorption. One-year treatment outcomes should be awaited to assess the full effect on wet weight, energy, and macronutrient absorption.

- B23 -

MACROPHAGE HETEROGENEITY IN THE MUSCULARIS EXTERNA OF THE HUMAN INTESTINE. N. Stakenborg (1), M. Delfini (1), E. Modave (1), T. Voet (2), A. Sifrim (2), A. D'Hoore (3), A. Wolthuis (3), G. Boeckxstaens (1) / [1] KUL - University of Leuven, Leuven, Belgium, TARGID, [2] KUL - University of Leuven, Leuven, Belgium, Department of Human Genetics, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Abdominal Surgery.

Introduction: Tissue resident macrophages (rMF) are a heterogeneous population of tissue supportive cells characterized by distinct gene expression programs. In the muscularis externa of the murine intestine, we reported that rMF are long lived and show specific phenotypes and functions depending on their anatomical niche. Depletion of rMF led to vasculature leakage and neuronal loss, demonstrating their central role as gatekeepers of intestinal homeostasis.
Aim: To characterize and generate a single cell atlas of the rMF populations in the muscularis externa of the human intestine.
Methods: Full thickness samples were collected from the descending colon of patients undergoing abdominal surgery (n=9) and the muscular layer was dissected. To uncover macrophage heterogeneity, the tissue was digested and CD45+ cells were sorted to perform single cell RNA sequencing. The sequenced data was analyzed with Seurat to perform cluster-specific marker identification. Slingshot and Monocle R packages were used for trajectory analysis.
Results: In the human muscularis externa, we identified 2 independent rMF populations; one expressing oligodendrocyte markers, such as PMP22) and the other expressing markers involved in lipid metabolism (f.e. ApoE). To infer if these two populations had an alternative endpoint of macrophage differentiation, we reconstructed their differentiation tree in silico. This trajectory analysis showed that monocytes differentiated into the two independent terminal populations. To validate the localization of these muscularis rMF populations, we performed confocal microscopy of a cleared whole mount muscularis tissue. 3D reconstruction showed that PMP22+ rMF were specifically located in the serosal layer. Finally, patient stratification based on age showed a change in the relative proportions of mature and progenitor populations.
Conclusions: We characterized two human intestinal rMF subpopulations both from a functional and localization point of view. This knowledge paves the way to investigate their respective role in gastrointestinal disorders.

- B24 -

DUODENAL MAST CELLS, BUT NOT EOSINOPHILS ARE HIGHER IN FUNCTIONAL DYSPEPSIA PATIENTS AS ASSESSED BY THE NOVEL LEUVEN INTESTINAL COUNTING PROTOCOL. P. Huyghe (1), M. Ceulemans (1), A. Cetin (1), L. Wauters (1), M. Carlson (2), G. De Hertogh (3), J. Tack (1), T. Vanuytsel (1) / [1] KU Leuven - University of Leuven, Leuven, Belgium, Translational Research Center in Gastrointestinal Disorders (TARGID), [2] Uppsala university, Uppsala, Sweden, Gastroenterology Research group, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Pathology.

Introduction: Functional dyspepsia (FD) is a gastrointestinal (GI) disorder characterised by upper abdominal symptoms in the absence of an organic cause evaluated by routine upper GI endoscopy. The Rome IV criteria make a distinction between two subtypes, postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS). Recent research has reported higher levels of eosinophils and mast cells in the duodenum of FD patients. Although these findings have been confirmed by several groups, conflicting results are found in literature, possibly due to a lack of uniformity on the counting procedure.
Aim: The aim of this study was to create a uniform counting method to standardise the eosinophil counting procedure. In addition, we aimed to assess differences in eosinophil and mast cell counts using this novel method and compare histological counts to eosinophil-derived neurotoxin (EDN) as a more objective marker of eosinophil presence.
Methods: Previously collected H&E and c-kit stained, encoded duodenal (D2) biopsy sections were counted by two independent assessors (A1 and 2) using two separate counting methods, the traditional microscope-based method and our novel software-based method. In the first, a Leitz Wetzlar Orthoplan microscope (40x objective, HPF: 0.264 mm^2) was used to count eosinophils and mast cells. In the latter, scanned tissue sections (Aperio CS2 slide scanner (Leica Biosystems, 40x magnification)) were counted using the Aperio ImageScope software (Leica Biosystems). Here, a fixed-size, circular region (0.264 mm^2) was drawn, wherein the intercryptal region, spanning from villus base to muscularis mucosae, was indicated, excluding crypts, glands, and blank spaces. For both counting methods, cells were counted in three non-overlapping fields of view. In addition, proteins were extracted from the duodenal biopsies of these HCs and FD patients, and EDN concentration was measured using ELISA (Diagnostics development). R (v4.2.2) was used to calculate the intraclass correlation coefficient (ICC) (irr package, model = twoway, type = consistency) and to perform the analysis using a paired or unpaired t-test or Wilcoxon signed-rank test, depending on normality.
Results: In total, tissue sections of 29 FD patients (24 female, mean ± SD age 32 ± 2 years, Rome IV) and 30 age- and sex-matched HCs (21 female, mean ± SD age 31 ± 2 years) were included. An improvement in ICC values was observed when comparing the eosinophil counts of two independent assessors between the microscopic counting method and software-based method (ICC=0.58, $p<0.0001$ and ICC=0.68, $p<0.0001$, respectively). Interestingly, similar Spearman

correlation coefficients (r) were observed comparing eosinophil counts via the software-based method and an objective eosinophil marker, EDN concentration in biopsy lysates, between both independent assessors. Here, significant and moderate correlation was found for HCs (A1: r=0.400, p=0.03 and A2: r=0.389, p=0.03), no correlation for FD patients (A1: r=0.089, p=0.65 and A2: r=-0.067, p=0.7) and a trend for a moderate correlation for both groups combined (A1: r=0.277, p=0.09 and A2: r=0.211, p=0.11). In contrast, performing the same analysis for microscopic-based eosinophil counts showed larger discrepancies between both assessors (HC; A1: r=0.324, p=0.08 and A2: r=0.239, p=0.2, FD; A1: r=0.338, p=0.08 and A2: r=0.160, p=0.4 and both groups; A1: r=0.337, p=0.009 and A2: r=0.208, p=0.1). Using this novel counting method, no significant differences were found in mean eosinophil numbers (± SD) comparing FD patients and HCs for both assessors (168 (±56)/mm² vs 172 (±70)/mm², p=0.6 and 81 (±35)/mm² vs 94 (±46)/mm², p=0.7, respectively), whereas mean mast cell numbers (± SD) were significantly higher in FD patients compared to HCs (322 (±97)/mm² vs 264 (±84)/mm², p=0.02).
Conclusions: Here, we have introduced a novel, software-based counting method demonstrating improved reliability compared to the traditional, microscopic counting method and showing more similarity between assessors in correlation with an objective eosinophil marker. Implementation of this new method showed differences in mast cell, but not eosinophil numbers. Adoption of this more reproducible protocol across centres will enhance comparability of outcomes in FD and potentially also eosinophilic gastrointestinal disorders.

- B25 -

DUODENAL CYTOKINE EXPRESSION IS LINKED TO EDN PRODUCTION IN FUNCTIONAL DYSPEPSIA DESPITE LIMITED ALTERATIONS IN THE LOCAL INFLAMMATION-RELATED PROTEOME. A. Cetin (1), M. Ceulemans (1), P. Huyghe (1), J. Tóth (1), L. Wauters (1), M. Carlson (2), J. Tack (1), T. Vanuytsel (1) / [1] KUL - University of Leuven, Leuven, Belgium, TARGID, [2] Uppsala university, Sweden, Gastroenterology Research Group.
Introduction: Functional dyspepsia (FD) is a common gastrointestinal (GI) disorder characterized by low-grade inflammation in the duodenal mucosa including eosinophil infiltration (Ceulemans et al. Frontiers Neuroscience 2022). Despite its major importance in the infiltration and activation status of eosinophils, the local cytokine profile in the duodenum remains underexplored. Eosinophil-derived neurotoxin (EDN) is an eosinophil granule released upon eosinophilic degranulation. However, its role in FD has not been studied. Proton pump inhibitors (PPI) are still the first line treatment in FD. The first prospective evidence for eosinophil-reducing effects in the duodenum as a therapeutic mechanism of PPIs in FD has been delivered (Wauters et al. Gastroenterology 2021), but their anti-inflammatory mechanism of action remains unclear. The Olink multiplex assay, based on the Proximity Extension Assay (PEA) technology, measures up to 92 inflammation-related human protein biomarkers (full list via https://olink.com) in various samples, and can give new insights.
Aim: The aim of this study was to assess differences in the expression of inflammation-related proteins in FD versus healthy volunteers (HV), which could play a role in the pathogenesis of FD. Besides, potential anti-inflammatory effects of a 4-week PPI treatment were assessed in FD patients compared to baseline. Finally, potential associations between duodenal EDN production and the expression of inflammatory proteins were evaluated.
Methods: FD patients who fulfilled Rome IV criteria were matched with HV and recruited to undergo upper endoscopy with duodenal biopsies. Procedures were repeated in FD patients after pantoprazole 40 mg OD for 4 weeks (‘on PPI’). After the extraction of proteins from duodenal biopsies, EDN concentration was measured with ELISA and inflammatory cytokine expression was analysed using the Olink Proseek Multiplex Inflammation I kit. A dual antibody recognition step was followed by qPCR detection. Next, data were obtained by using a pre-processing normalization procedure and output data was presented as normalized protein expression (NPX) such that a higher NPX value corresponds to a higher protein expression. Each PEA measurement has a lower limit of detection (LOD) based on negative controls included in each run. For each individual protein assay, values below the limit of detection (LOD) were replaced with the respective LOD, which can be found on the manufacturer’s website. Analyses were conducted in R studio with (non-) parametric tests depending on normality and calculation of Spearman’s correlation coefficient (r).
Results: In total, 29 FD patients (24 female, mean ± SEM age 31 ± 2 years) and 29 age- and sex-matched HV (20 female, age 33 ± 3 years) were included. There were no significant differences in protein expression between HV and FD at baseline. CCL4 (4.57 ± 0.14 vs. 4.27 ± 0.20; p= 0.04), AXIN1 (3.54 ± 0.23 vs. 2.91 ± 0.28; p= 0.036) and IL-6 (0.41 ± 0.05 vs. 0.28 ± 0.02; p= 0.007) decreased in FD after PPI therapy. In contrast, a significant increase was found for IL-18 in FD on-PPI vs. baseline (9.43 ± 0.20 vs. 9.11 ± 0.18; p= 0.038). No significant differences for EDN were found in HV off vs. FD off (257.80 ± 21.78 vs. 278.30 ± 29.41; p= 0.84) and in FD on PPI vs. baseline (283.80 ± 36.74 vs. 278.30 ± 29.41; p= 0.73). There were significant correlations between EDN and CCL4 (r= 0.52; p= 0.004), as well as EDN and IL-33 (r= 0.52; p= 0.004) in FD at baseline, but not in HV and FD on PPI. In addition, the correlations between EDN and MCP-2 (r= 0.38; p= 0.048), as well as MCP-4 (r= 0.55; p= 0.002) in FD at baseline also persisted in FD on PPI (MCP-2: r= 0.61 p= 0.0009; MCP-4: r= 0.74; p< 0.0001) but were absent in HV.
Conclusions: In FD patients, subtle alterations in protein expression after PPI therapy were found using a multiplex protein analysis, although it remains unclear how they relate to the eosinophil infiltration reported in literature. Moreover, CCL4, a pro-inflammatory chemotactic cytokine, along with eosinophil chemoattractants IL-33, MCP-2 and MCP-4 were associated with duodenal EDN levels in patients, suggestive of a mechanism of activation, although protein levels of

these eosinophil-inducers were unchanged in FD. Lastly, MCP-2 and -4 could also be involved in the immunomodulatory effects of PPI on eosinophils.

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SHORT-TERM OUTCOME OF MEDICALLY REFRACTORY CHRONIC CONSTIPATION EVALUATED WITH HIGH-RESOLUTION COLONIC MANOMETRY. A. Verheyden (1), A. Blomsten (2), J. Pannemans (3), W. Verbeure (3), H. Törnblom (2), T. Vanuytsel (3), J. Tack (3) / [1] KUL - University of Leuven, Leuven, Belgium, Gastroentrology, [2] Sahlgrenska University Hospital Gotheburg, Gothenburg, Sweden, Gastroenterology and Hepatology, [3] KUL - University of Leuven, Leuven, Belgium, Gastroenterology.

Introduction: Patients with medically refractory chronic constipation are eligible for subtotal colectomy with ileorectal anastomosis (SC-IRA) when normal defecatory function and colonic inertia are confirmed.
Aim: The aim of this study was to evaluate the outcome of patients with severe refractory constipation treated surgically (SC-IRA) or conservatively after investigation with high-resolution colonic manometry (HRCM). The primary endpoint is the constipation quality of life score (PacQol) subscale satisfaction with stool pattern. Secondary endpoints include constipation symptom (PacSym) scores, other PacQol subscales, colonic transit time, and anorectal manometry (ARM) with balloon expulsion test (BET) results.
Methods: 126 refractory constipation patients, who underwent extensive work-up including colonic pellet transit time, ARM with BET (50mL balloon expelled within 1min.), and HRCM with intracolonic administration of bisacodyl between 2015 and 2019, were contacted to fill out an extensive follow-up questionnaire, including PacSym, PacQol, depression (Patient Health Questionnaire; PHQ9), anxiety (General Anxiety Disorder; GAD7), pain-related anxiety (Pain Anxiety Symptoms Scale; PASS), physical and mental health (PROMIS10).
Results: 71 patients consented and were divided into 3 groups based on treatment after work-up: conservative (n=36), subtotal colectomy for demonstrated colonic inertia (n=9), and subtotal colectomy in absence of colonic inertia (n=26). Follow-up data was retrieved on average 4 years after HRCM and 3 years after SC-IRA (range 0-6 years). Prior to the work-up, participants (3 men, mean age 45 ± 14 y) had tried on average 9 ± 3 drug treatments. The average transit time was 113 ± 30 h and was significantly higher in the inertia group compared to both conservatively treated participants ($p=0.0005$) and surgically treated participants without inertia ($p=0.001$). No statistically significant differences were found between the 3 treatment groups in terms of ability to expel a balloon ($p=0.80$) and rectal sensitivity based on ARM ($p=0.62$). Both the surgical group without inertia and the inertia group showed significantly higher satisfaction on the PacQol stool pattern satisfaction scale than the conservative group (both $p<0.005$), while there was no statistically significant difference between the surgical groups. Other PacQol subscales were also statistically significantly different between the 3 treatment groups, with better outcomes for the surgical group without inertia compared to the conservatively treated patients for mean PacQol ($p=0.0021$) and its subscales of physical discomfort ($p=0.043$) and worries & concerns ($p= 0.0016$). PacQol psychosocial discomfort was significantly lower in the surgical group without inertia compared to the inertia group ($p=0.038$). For the other PacQol subscales, no significant differences were found between the surgical group with inertia and the one without inertia. No statistically significant differences were found between the 3 treatment groups for the PacSym score ($p=0.25$) and its subscales of abdominal ($p=0.44$), rectal ($p=0.60$), and stool scores ($p=0.066$). Moreover, there was no statistically significant difference in depression scores between the 3 treatment groups ($p=0.30$). Patients without colonic inertia had statistically significantly lower anxiety scores compared to conservatively treated participants ($p=0.014$). Depression and anxiety scores were positively correlated to PacQol satisfaction scores ($r=0.36$, $p=0.004$ and $r=0.36$, $p=0.003$ respectively). We did not find a statistically significant difference in pain-related anxiety ($p=0.24$) and physical health scores ($p=0.93$) between the 3 treatment groups, although the mental health scores were statistically significantly higher for the surgically treated participants without inertia compared to the conservative group ($p=0.0498$). Medication usage was higher in surgically treated participants with inertia compared to those treated conservatively ($p=0.018$), driven by drugs targeting diarrhea, nausea, sleep, and pain.
Conclusions: On average 4 years after detailed investigation for severe refractory constipation, satisfaction with the stool pattern was higher in those referred for subtotal colectomy, regardless of colonic inertia status, compared to those treated conservatively, with a clear influence of depression and anxiety. Our study illustrates that there are multiple determinants of outcome in severe refractory constipation, that should be evaluated with care for future treatment choices in refractory constipation.

- B27 -

EFFECT OF A HISTAMINE RICH MEAL VERSUS A LOW HISTAMINE MEAL ON URINARY HISTAMINE EXCRETION. B. Broeders (1), L. Van Aelst (2), J. Tóth (3), C. Matthys (4), J. Tack (5) / [1] KUL - University of Leuven, Leuven, Belgium, TARGID, [2] KUL - University of Leuven, Leuven, Belgium, Faculty of Medicine, [3] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Faculty of Medicine, [4] KU Leuven - University of Leuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism, [5] University Hospitals Leuven, KU Leuven, Belgium, Department of Chronic Diseases and Metabolism.

Introduction: Functional dyspepsia (FD) and irritable bowel syndrome (IBS) are disorders that affect approximately 20% of the population. One of the proposed pathophysiological mechanisms in these conditions is a loss of mucosal integrity, associated with low-grade inflammation and food-induced mast cell activation. To date, confocal laser endomicroscopy to monitor allergy-like reactions to luminal food protein application, or a wheal-and-flare-like reaction to submucosal injection of food proteins have experimentally been used to demonstrate allergy-like food responses in these patients. Compared to these complex methods, urinary histamine measurement may provide an elegant and non-invasive tool to detect such food reactions in FD and IBS.

Aim: In this pilot project we assessed the ability to detect an increase of urinary histamine and n-methylhistamine after ingestion of food with different histamine content.

Methods: Healthy volunteers were recruited to ingest a histamine rich meal (HRM) or low histamine meal (LHM) on two different days with one week in between, in a cross over fashion. All volunteers filled out the upper gastrointestinal ROME-IV diagnostic questionnaire to confirm the absence of disorders of gut-brain interaction. Volunteers came to the hospital fasted and received a standardized breakfast (pancake, brown sugar, water). After two hours participants were asked to empty the bladder before they consumed the study meal. After finishing the meal participants collected all urine and filled out symptom questionnaires of 10 gastrointestinal symptoms (VAS 0-4) for 4 hours. ELISA analysis of urinary histamine and n-methylhistamine were performed in accordance with the manufacturer's instructions. Data are shown as mean ± standard deviation. Statistic tests were done using a paired T-test or two-way ANOVA as appropriate.

Results: We recruited 10 healthy volunteers (70% female) with an average age of 23.8 ± 5.05 years and an average body mass index (BMI) of 21.3±1.55. All participants finished the whole meal. Urinary output was similar after the HRM and LHM (respectively 577±167 mL and 540±128 mL, p=0.605). There was no difference in urinary N-methylhistamine excretion between the HRM and LHM (respectively 34.5±8.8 µg/g creatinine vs 36.3±10.3 µg/g creatinine, p=0,779). Urinary excretion measures of histamine were below the detection limit in the majority of samples, excluding this aspect from statistical analysis. Overall symptom scores did not differ significantly after the HRM and the LHM. Only at 15 minutes postprandially, higher scores were found for postprandial fullness after the HRM (mean difference of 0.4 [95% CI 0.01 – 0.79], p=0,038).

Conclusions: In healthy volunteers' administration of food with high histamine content compared to food with low histamine content does not increase urinary N-methylhistamine excretion. Ingestion of a histamine rich meal was associated with a transient postprandial increased feeling of excessive fullness and did not induce a significant rise in postprandial symptoms.

CASE REPORTS

- C01 -

SEVERE ABDOMINAL PAIN AS A PRESENTATION OF NEUROBORRELIOSIS. V. Chua (1), A. Tourmous (2), R. Mazzoleni (3), S. Huvelle (4), R. Ntounda (5), N. Schoofs (6), B. Van Houte (6), F. Salomez (7) / [1] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, Gastroenterology, [2] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, Pneumology, [3] CHR, Namur, Belgium, Neurology, [4] CHR, Namur, Belgium, Clinical Biology, [5] CHU Saint-Pierre, Brussels, Belgium, Gastroenterology, [6] CHR, Namur, Belgium, Gastroenterology, [7] CHR, Namur, Belgium, Intensive care.

Introduction: Lyme disease is a very common zoonosis caused by the Borrelia bacterium. Diagnosis of Lyme disease can be difficult due to the wide variations of clinical manifestations. After reviewing the literature, we realised that abdominal pain as a presentation mode has only been described in a few case reports. If untreated, it can evolve into life-threatening neuroborreliosis, which is a rare and often misdiagnosed neurological condition. The incidence of Lyme disease is increasing and the proportion of cases evolving into neuroborreliosis in Belgium is 26.5% (1) (and up to 46% in Europe depending on the region), which is why we would like to assess the importance of recognising neuroborreliosis when encountered. The main manifestations of neuroborreliosis are meningitis, cranial neuritis and radiculoneuritis. Neuroborreliosis is not yet included in the differential diagnosis of severe abdominal pain. We report a very rare case of neuroborreliosis with abdominal distension and severe abdominal pain as first symptoms.
Case Report: A 65-year-old man presented to the emergency department with abdominal pain and asthenia as his main complaints. He also suffered from nausea, vomiting and constipation, with no effect of laxative treatments. His medical history included cardiac ischaemia, hypertension and hypercholesterolaemia. There was no history of recent foreign travel. An abdominal CT scan was performed and showed colon distension and faecal stasis with no signs of obstruction. The patient was then hospitalised for pain management and further investigations. During hospitalization, the patient complained of sudden diplopia and progressive weakness of the lower limbs. Brain CT scan and MRI showed no explanation for the neurological symptoms. Electromyography showed bilateral neuropathy in the lower limbs. A lumbar puncture was performed and showed pleocytosis (622 cells/mm3), hyperproteinorachia (2.61g/L), hyperlactatemia (4 mmol/L). CSF PCR analysis were negative for N. meningitidis, CMV, HSV 1 and 2, and positive for B. Garinii. The patient was treated with intravenous acyclovir and ceftriaxone. Acyclovir was stopped 24 hours later due to acute renal failure The neurological condition of the patient, including abdominal pain and distension, began to recover after 48 hours of treatment with ceftriaxone at a dosage of 2g per day for a total of 21 days. After these three weeks, only mild abdominal pain remained.
Discussion: Abdominal pain and distension are a very rare mode of presentation for neuroborreliosis. A few cases are described in the literature. Autonomic dysfunction is often suggested and is the likely explanation in our case. Although the pathophysiology of the abdominal distension in neuroborreliosis remains to be studied, neuroborreliosis should be considered when abdominal distension and pain are encountered. The main manifestations of neuroborreliosis tend to be revisited (2), and we think it is important to reassess the possibility of less common manifestations.
Conclusion: Although il is a rare diagnosis, neuroborreliosis should be considered in the differential diagnosis of abdominal pain and bowel distension without other obvious causes. As the incidence of Lyme disease is increasing over the years and as Belgium is an endemic area for Borrelia infection, it is important to assess the frequency of these abdominal manifestations.
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- C02 -

CEREBRAL AIR EMBOLISM AS A COMPLICATION OF ESOPHAGOGASTRODUODENOSCOPY. H. Buelens (1), M. Van Parijs (2), E. Ali (3), P. Abrams (4), F. Van De Mierop (5), I. Maurissen (5) / [1] GZA Sint-Vincentius, Antwerp, Belgium, Antwerp, Belgium, Gastroenterology, [2] GZA Sint-Vincentius, Antwerp, Belgium, Antwerp, Belgium, Intensive care, [3] GZA Sint-Vincentius, Antwerp, Belgium, Antwerp, Belgium, Emergency medicine, [4] GZA Sint-Vincentius, Antwerp, Belgium, Antwerp, Belgium, Endocrinology, [5] GZA Sint-Augustinus, Antwerp, Belgium, Antwerp, Belgium, Gastroenterology.

Introduction: Cerebral air embolism is a rare complication following gastrointestinal endoscopic investigations. Symptoms are cardiovascular or pulmonary (hypoxia, hypotension, collapse, cardiac arrest etc.) and deterioration of neurological functions. Treatment includes supportive therapy and hyperbaric oxygen. (1, 2) Decreased neurological status after endoscopy should never be solely attributed to the effects of sedation. Because of potential mortality, it is crucial to recognise this complication and take appropriate action.

Case description: An 85-year-old woman presented with one episode of hematemesis. The patient's history included liver cirrhosis (alcoholic etiology), hypertension, hypercholesterolaemia and breast ductal adenocarcinoma. She takes propranolol for prevention of variceal bleeding. She had a DNR-1 code. The patient was hemodynamically stable with a slightly painful epigastric palpation. Lab results showed a hemoglobin of 13,5 g/dl, other tests were also normal. She had a prolonged QTc interval of 506ms, taking trazodone, citalopram and zolpidem. Therapy included fluid and pantoprazole 40mg twice a day intravenously. Abdominal ultrasound showed liver cirrhosis. Esophagogastroduodenoscopy reveals remarkable esophagitis and a distal oesophageal bleeding (without a direct visualisation of varices or the bleeding origin). At the end of the examination, the patient was suddenly not responsive, despite not receiving any sedatives. Therapy was started with a mayo cannula and oxygen. Vital signs and glycaemic level were normal. She had a Glasgow Coma Scale of 3/15 with miotic pupils and eyes deviated to the left. Although no convulsions were seen, lorazepam 2mg was administered to treat possible underlying epileptic activity. CT scan showed multiple air embolisms in both hemispheres. Somatostatin was started to treat possible variceal bleeding. Although non-responsive, she was spontaneously moving her legs. Hyperbaric oxygen therapy was considered but decided against for multiple reasons. Later there was some neurological recovery; following commands, minimal speech and left-sided hemineglect. Sudden respiratory deterioration with pneumothorax occurred, treated by needle decompression. Cardiac ultrasound showed no signs of a patent foramen ovale or other transseptal passage. Placing the patient's comfort first, only oxygen was given. The left sided hemiparesis persisted. Her general condition further decreased. A DNR-3 code was introduced and palliative sedation was started. Sadly, the patient died.
Discussion: Air embolism is more frequently associated with ERCP but can also happen during other gastrointestinal endoscopy such as esophagogastroduodenoscopy with an incidence of around 0,00056%. (1-3) The proposed mechanism in this patient is insufflation of air, entering through the esophageal varix into the portal venous system. For a cerebral air embolism to occur, an intracardiac shunt could be present, but was not seen on echocardiography. Other mechanisms mentioned in previous literature include intrapulmonary shunts (often seen with chronic liver disease), passage from the superior caval vein to the cerebral veins by retrograde flow etc. (1-2, 4). No autopsy was performed in discovering the exact mechanism. Therapy options are supportive (Trendelenburg or left lateral decubitus position, oxygen, IV fluids, vasopressors) and hyperbaric oxygen. (1-3) Using carbon dioxide for insufflation can lower the risk of an air embolism. (3, 5) A pre-endoscopic echocardiography could prevent some cases but is not cost-effective.
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- C03 -

CYP2C19 METABOLISM IN PEPTIC ULCER DISEASE. L. Janssens (1), S. Vege (1) / [1] Mayo Clinic, Rochester, United States, Gastroenterology.

Case Report: A 53-year-old woman presented to the clinic with worsening epigastric pain and heartburn symptoms. Her relevant medical history included gastroesophageal reflux disease (GERD) status post Nissen fundoplication (2000) and re-do fundoplication (2016), recurrent Clostridium difficile colitis, COPD with active nicotine use, and chronic pain syndrome on opioids. Her complex symptomatology with chronic abdominal pain and heartburn had resulted in 39 emergency department visits and 16 computed tomography (CT) scans of the abdomen in the past four years, usually without any findings of organic disease. Current medical management included esomeprazole twice daily, dicyclomine, duloxetine, nortriptyline, oxycodone, polyethylene glycol 3350, and naloxegol. On evaluation, she endorsed worsening epigastric pain limiting oral food intake. Physical examination revealed diffuse mild tenderness over the whole abdomen. Her most recent upper endoscopy was performed 6 months earlier and was unremarkable. Due to her persistent and worsening complaints of epigastric abdominal pain, she underwent a repeat upper endoscopy while taking esomeprazole 40 mg twice daily. This revealed four new acute-appearing antral ulcers, the largest measuring over 1 cm in diameter. Biopsies were obtained on two separate occasions and did not show helicobacter pylori. The patient denied taking any non-steroidal anti-inflammatory drugs (NSAIDs). Further laboratory work-up showed elevated fasting gastrin of 975 pg/mL (normal <100 pg/mL), elevated chromogranin A of 660 ng/mL (normal <93 ng/mL), negative anti-parietal cell antibodies, and normal vitamin B12 levels. Gastric pH was measured at 2,5 (while on esomeprazole). CT with triple phase, endoscopic ultrasonography, and 68Ga-DOTATATE Positron Emission Tomography were performed but did not reveal evidence of gastrinoma. Cytochrome P450 2C19 (CYP2C19) genotype testing was pursued, confirming the presence of ultrarapid metabolizer status. Esomeprazole was switched to rabeprazole, resulting in near resolution of the ulcers at 4 weeks follow-up and improvement in symptoms. Peptic ulcer disease (PUD) that occurs in the absence of typical precipitating factors (NSAIDs, Helicobacter Pylori) should raise suspicion for an underlying gastrin-secreting

malignancy, also known as Zollinger-Ellison syndrome (ZES). While gastrin levels >1000 pg/mL (in the presence of low gastric pH) are often cited as a diagnostic criterion for ZES, up to 66% of patients with ZES have gastrin levels <1000 pg/mL. However, in this case, no imaging evidence was found to support a diagnosis of ZES. Rather, our patient was found to be a CYP2C19 ultrarapid metabolizer which is found in approximately 5% of Caucasian and African American populations. While ZES cannot completely be ruled out with negative imaging studies, the objective improvement of our patients' PUD after switching from esomeprazole to rabeprazole argues against ZES in this case. CYP2C19 is involved in the metabolism of all proton pump inhibitors (PPIs) except for rabeprazole, which is primarily cleared non-enzymatically. New onset PUD that occurs in the absence of typical risk factors (especially while on PPI treatment) warrants evaluation for ZES and CYP2C19 phenotype status. PUD or objective GERD in patients with ultrarapid CYP2C19 metabolism should be treated with rabeprazole.

- C04 -

A CASE OF A YOUNG GIRL WITH TUBERCULOSIS, THAT MIMICS CROHN'S DISEASE. E. Levy (1), K. Huysentruyt (2), F. Mouchet (3), A. Dreesman (4) / [1] CHU Saint-Pierre, Brussels, Belgium, Paediatric gastroenterology, [2] KidZ Health Castle, UZ Brussel, Jette, Belgium, Paediatric gastroenterology, [3] CHU Saint-Pierre, Brussels, Belgium, Paediatric pulmonology, [4] CHU Saint-Pierre, Brussels, Belgium, Paediatric Pulmonology-Immunology.

Case Report: A seven-year-old girl presented with a six months history of intermittent fever episodes without apparent cause, as well as appetite and weight loss and abdominal pain. Stools varied between Bristol type 2-4 without presence of blood or mucus, there was no associated vomiting. Papular skin lesions were noted on the upper and lower limbs. Blood analysis, with a six week interval, showed marked systemic inflammation with CRP 40-50 mg/L (<5), sedimentation 103-120 mm/h(<20), platelets 490-470 x10^3/µL (150-440)and normal white blood cell count 6.0 x10^3/µL (6.00-14.50). There was as well a microcytic anaemia (11.3 g/dL (11.5-15.5), MCV 68-68 fL (75-87), iron 27-28 µg/dL (28-140), ferritin 46 50 µg/L (12-140). Further there was a normal albumin 40-45 g/L (38-54), normal lipase (17 UI/L (13-60) and liver enzymes 32- 28 AST (GOT) UI/L(<41)/ 17-13 ALT GPT UI/L (<28), bilirubin total 0.4 mg/dL (<1.2), 46-38 gamma-GT UI/L (5-32). Stool analysis was negative for bacteria and parasites, but faecal calprotectin was elevated (298 µg/g, nl <50). There was no evidence of hepatic involvement (normal liver enzymes, lipase, bili, albumin etc) and serologies for hepatitis A, B, CMV EBV and HIV were negative. Total IgG A and anti-transglutaminase antibodies IgA were within normal range. Abdominal ultrasound showed a string of lymph nodes supra hilar of the liver as well as minimal ascites in the pelvic region. The quantity of ascites was too small to be punctured. A gastro-colonoscopy was performed to exclude Crohn's disease: it was macroscopically and microscopically normal. MRI enterography was proposed but refused by the parents. Screening for tuberculosis (TB) was performed in parallel and showed a positive tuberculosis skin test (TST), positive IGRA (interferon gamma release assay) as well as a slightly enlarged mediastinum on chest X ray in the absence of pulmonary lesions. Smear test and PCR for Mycobacterium tuberculosis came back negative on broncho-alveolar lavage as well as gastric lavage (x3) and intestinal biopsies, but the clinical picture was sufficiently suggestive for TB to start empirical TB treatment with classical quadritherapy (Isoniazid, Rifampicin, Pyrazinamide and Ethambutol), while awaiting definitive culture results. Lymph node biopsy was proposed in order to obtain microbiological confirmation but also refused by the parents. In the literature there is no guideline, how to proceed in children concerning follow-up of faecal calprotectin in similar cases. However, adult literature describes elevated faecal calprotectin in cases of abdominal TB with normalisation two months after initiation of TB treatment. In this case the faecal calprotectin normalized (4 µg/g (<50)) after two months of treatment, however the patient was still anaemic 10.7 g/dL 11.5-15.5, MCV 67 fL] 75-87). Systemic inflammation also progressively resolved (CRP 11.4 mg/L (<5), sedimentation 47 mm/h (<20), platelets 444 x10^3/µL (150-440), white blood cell count 8.00 x10^3/µL (6.00-14.50)) In the meantime the child recovered from the first weeks of treatment onwards, with a normalisation of appetite and stools, as well as progressive weight gain and resolution of abdominal pain. Fever remitted entirely in the first weeks of treatment. Repeat abdominal ultrasound showed micronodular splenic lesions and resolution of ascites (at 1 months of treatment). As described in adult literature, this case shows the difficulty in differentiating between Crohn's disease and tuberculosis. Although definitive cultures on respiratory as well as digestive samples failed to show microbiological evidence of tuberculosis, the clinical picture was sufficiently suggestive to start TB treatment and treatment response was in favour of TB. To conclude, abdominal tuberculosis may mimic Crohn's disease in children. Chest imaging as well as obtaining specimens from all relevant sites for Mycobacterium tuberculosis culture/histology is warranted in case of clinical suspicion of TB especially in case of positive TST and/or IGRA. Elevated faecal calprotectin does not differentiate between inflammatory bowel disease and abdominal TB.

- C05 -

SKIN RASH AFTER VEDOLIZUMAB IN CROHN'S DISEASE. V. Vandebroek (1), S. Arnaert (1), M. Cool (1), L. Bossuyt (2), D. Persyn (1), G. Lambrecht (1), G. Deboever (1) / [1] AZ Damiaan, Oostende, Belgium, Gastroenterology, [2] AZ Damiaan, Oostende, Belgium, Dermatology.

Case Report: Inflammatory bowel disease (IBD) is a chronic immune-mediated disorder comprising two main entities. Colitis ulcerosa and Crohn's disease mainly affect the gastrointestinal tract. However, extra-intestinal manifestations are common and can include the skin, as well as the eyes, heart, lungs, kidneys and hepatobiliary system. IBD patients develop cutaneous manifestations in 10 to 15% of all cases. Erythema nodosum is a subcutaneous and nodular rash on the lower extremities occurring more commonly in females than males. It is self-limiting and coincides with IBD activity (1). Other associated cutaneous manifestations are pyoderma gangrenosum, Sweet's syndrome, oral aphthous lesions and infusion related reactions. We present the case of a 19-year-old patient diagnosed with Morbus Crohn last year. At diagnosis she underwent a colonoscopy that showed pancolitis and terminal ileitis. Faecal calprotectin at diagnosis was >1000µg/g. Treatment with vedolizumab was initiated by including the patient in the LOVE-CD study. Under vedolizumab endoscopic remission was obtained. Unfortunately, therapy needed to be stopped due to intolerance (infusion reactions), 8 weeks prior to current presentation. At present intestinal symptoms seem under control, however, the patient does report a pruritic pustular rash at the hands and wrists. A nodular rash with purple discoloration was noted at the upper right thigh. The patient was sent to the dermatologist to exclude erythema nodosum or (remainder of an) infusion related reaction. Dermatological examination showed pathognomonic burrows at the hands. A more thorough history revealed her boyfriend being treated for scabies a few months before.
Although Crohn's disease and its treatment are associated with skin disorders such as erythema nodosum, pyoderma gangrenosum, infusion reactions…, it remains important to maintain a broad differential diagnosis. A thorough history and physical exam has to be performed, with referral to dermatology if needed. In this case the skin rash could mimic erythema nodosum or an infusion related reaction, the adverse effects on vedolizumab and the omission of therapy the last few weeks were other reasons to think about IBD related cutaneous manifestations. There is no published research about the epidemiology of scabies in IBD patients, or whether immunosuppressive treatment causes an increased prevalence of scabies in IBD patients. A more extreme clinical entity is Scabies norvegica, where the mites can multiply to millions in immunocompromised patients. Patients with uncontrolled IBD are deemed at increased risk for this fulminant infection (2). On the other hand, the incidence of scabies has been increasing rapidly the last few decades, especially in young adults (3). These are the patients who also have Crohn's disease treated by biological therapy.
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- C06 -

SPLENIC ANGIOSARCOMA WITH HEPATIC METASTASIS: A RARE CAUSE OF HEPATIC FAILURE. I. Dirven (1), L. Braeckeveldt (1), H. Reynaert (1), P. Lefesvre (2), F. Vandenbroucke (3), M. Surmont (1) / [1] UZ Brussel, Jette, Belgium, Gastroenterology, [2] UZ Brussel, Jette, Belgium, Pathology, [3] UZ Brussel, Jette, Belgium, Radiology.

Case Report: We present the case of a 75-year-old woman referred for a liver biopsy. In her medical history, she had hypertension, well controlled with an ACE-inhibitor and a beta-blocker. Seven months prior to referral, she started to have B symptoms, including fatigue, weight loss and anorexia. A CT scan showed multiple splenic and hepatic nodules. Additional MRI imaging was most suggestive for multiple haemangiomata. A CT scan of the lumbar vertebral column three months later because of back pain revealed multiple new bone lesions that were suspect for bone metastases or multiple haemangiomata on subsequent MRI imaging. Her primary physician referred her to the haematology department. The work up for multiple myeloma and lymphoma with a lumbar puncture was negative. A PET-CT showed FDG-positive lesions in spleen and liver, and she was referred to our gastro-enterology service for a biopsy of a hepatic FDG-positive lesion. At the time of admission, there was progressive hepatic failure with increased bilirubin and INR and with low platelets and hyponatremia. Tumour markers CEA, CA 19.9, alfa-foetoprotein were normal. Immunohistochemical and histopathological results confirmed a metastatic lesion originating from a primary splenic angiosarcoma. She was unfit for chemotherapy because of rapidly progressive hepatic failure. There was clinical deterioration with fatal outcome shortly after.
Splenic angiosarcoma is a rare type of sarcoma with an annual incidence of 0.2/million. However, it remains the most common primary non-lymphoid, non-hematopoietic malignant tumour of the spleen. There is a very high metastatic risk of 69-100%, primarily to the liver. There are no specific diagnostic clinical or biochemical signs. Differentiation on imaging is challenging since imaging shows an overlap with other (benign) vascular lesions such as haemangiomata. Histopathological and immunohistochemical tissue analysis is therefore essential for diagnosis, but biopsies obtained by punction may lead to seeding of the tumour cells and rapid development of metastases. A splenic angiosarcoma has a very poor prognosis with a median overall survival of 5-6 months. In early stages, splenectomy can prolong median survival to 14 months. So, whenever possible splenectomy is advised for both diagnostic and therapeutic goals. Chemotherapy is often based on regimens for other (angio)sarcomas, but none have shown a significant effect on overall survival. However, randomised prospective studies in this setting are not feasible because of the aggressive character and rarity of

the disease. Based on imaging, the lesions in our patient were too quickly labelled as being benign haemangiomata. She developed bone metastasis and hepatic failure during the diagnostic delay of seven months.
The key points of this case are to remember that B symptoms and rapidly evolving lesions of the spleen and liver should always be alarming even if they look like benign lesions on imaging modalities. Histology is essential in diagnosis since radiographic differentiation between a benign haemangioma and angiosarcoma is often impossible. Splenic angiosarcoma is rare but sometimes we have to look for the zebra in a herd of horses.

- C07 -

AN UNUSUAL CAUSE OF VOMITING IN PREGNANCY: BROAD LIGAMENT HERNIA, FROM DIAGNOSIS TO MANAGEMENT. A. Pavlidi (1), R. Chapusette (2), M. Arvanitakis (1) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, [2] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Radiology.

Case Report: Nausea and vomiting are common experiences in pregnancy, affecting 70–80% of all pregnant women. However, the differential diagnosis at admission is often challenging due to overlapping symptomatology. If clinical suspicion, it is essential to provide appropriate investigations to these patients in order to exclude intestinal obstruction which is rare but associated to maternal and foetal mortality. We report the case of a 35-year-old woman admitted to the hospital at 27 weeks and 3 days of gestational age with a clinical picture of intestinal obstruction. An abdominal ultrasound was initially made confirming the presence of paralytic ileus but without any evident cause. Thereafter, an emergency abdominal magnetic resonance (MRI) was performed showing an internal hernia at the level of the left broad ligament, responsible for pathological dilation of the small bowel loops without any signs of mesenteric ischemia. A conservative treatment was firstly attempted with a favourable outcome: spontaneous resolution of the ileus and resumption of intestinal transit three days after admission. The patient was thus discharged from the hospital five days after admission, and she was able to safely deliver an infant at term.
This case highlights the importance of early identification of intestinal obstruction during pregnancy. Herniation through the broad ligament is rarely reported. To our knowledge, this is the second reported case of internal hernia through a defect in the broad ligament in a pregnant woman. The difficult task is selecting a radiological tool for evaluating these patients. Abdominal MRI seems to be a useful, safe and detailed diagnostic tool for small bowel obstruction in pregnant women. Subsequently, the early abdominal MRI has a crucial role both in diagnosis and in consequent multidisciplinary management.

- C08 -

CASE REPORT: SQUAMOUS CELL CARCINOMA AFTER RADIOFREQUENCY ABLATION FOR BARRETT'S DYSPLASIA. S. Bouhadan (1), S. Krishnadath (2), P. Dewint (3), A. Jauregui Amezaga (2), E. Macken (2) / [1] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology, [2] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology, [3] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology.

Introduction: Radiofrequency ablation (RFA) is an effective endoscopic treatment of dysplasia in Barrett. We describe a case of a patient developing a squamous cell carcinoma in the neosquamous epithelium after ablation.
Case presentation: A 56-year-old female was seen for surveillance endoscopy in August 2022. In 2011, a short segment Barrett's oesophagus was diagnosed. (Prague Classification C0M1) At that time histology showed high grade dysplasia. with p53 over-expression. This was not confirmed on subsequent endoscopies. Surveillance of Barrett's oesophagus was done regularly. Biopsies showed low grade dysplasia, p53 positive, but never high-grade dysplasia. In April 2019 the patient underwent radiofrequency ablation [RFA (HALO 90)], further sessions with HALO 60 for three more times. A follow-up gastroscopy in November 2021 was performed, biopsies showed non-dysplastic neo-squamous epithelium with no over-expression of p53. In September 2022- ten months later- a gastroscopy was performed. This time a lesion was seen between in the ablated area just above the neo-z line. Two short tongues of Barrett were also seen, separate from the lesion. Histology characterized the lesion was characterized as a squamous carcinoma. (carcinoma in situ) with strongly over-expression of p53.
Management and Outcome: Endoscopic submucosal dissection was performed. Histological analysis of the ESD specimen showed a poorly differentiated conventional squamous cell carcinoma, with invasion of the muscularis mucosae and infiltration into the submucosa. Lymphovascular invasion was present. Based on the findings it was staged as pT1bG3L1V1. PET/CT showed no metastasis. Patient was unfit for surgery due to chronic respiratory failure and chemoradiation therapy was suggested.

- C09 -

ATEZOLIZUMAB/BEVACIZUMAB: PUSHING THE BOUNDARIES IN HCC TREATMENT. C. Brackenier (1), J. Dekervel (2), J. Pirenne (3), P. Cuyle (4), C. Verslype (2) / [1] KUL - University of Leuven, Leuven, Belgium, Gastroenterology, [2] KUL - University of Leuven, Leuven, Belgium, Gastroenterology - Digestive Oncology, [3] KUL - University of Leuven, Leuven, Belgium, Abdominal Transplantation Surgery, [4] Imelda Hospital, Bonheiden, Belgium, Gastroenterology - Digestive Oncology.

Case description: A 66-year-old man was followed for cryptogenic cirrhosis (Child A5, MELD 9). His medical history consisted of arterial hypertension, lung empyema and colonic polyposis. At a surveillance ultrasound a nodule in segment 4 was found. A magnetic resonance imaging (MRI) revealed a hypervascular lesion with maximal diameter of 7.2 cm without macrovascular invasion in segment 4 and two dysplastic small lesions without malignant features on the background of a cirrhotic liver with signs of portal hypertension. The suspicious lesion was biopsied, and the diagnosis of HCC was confirmed by histopathology. Alpha-foetoprotein (alfaFP) was not elevated and no extrahepatic metastasis were seen on computed tomography (CT) of thorax and abdomen. Gastroscopy showed oesophageal varices for which endoscopic ligation was performed. Patient was considered outside the Milan criteria and no immediate candidate for liver transplantation (LTX). Surgical resection was no option given the clinically significant portal hypertension and the limited functional liver capacity on mebrofenin scan. Downstaging was attempted performing selective internal radiation therapy (SIRT) in segment 4 with only a moderate effect. The tumor had minimally enlarged with maximal diameter up to 7.8 cm and there was some, but only minimal, central necrosis of the tumor, together with a rise in alfaFP. Therefore, systemic therapy, consisting of atezolizumab/bevacizumab, a combination of an immune checkpoint inhibitor (anti-PD-L1) and an antiangiogenic (anti-VEGF) monoclonal antibody, was started eight months after diagnosis. Two cycles were administered. Systemic therapy was discontinued because of elevations of creatine kinases (CK), creatine kinase-MB (CK-MB) and troponins. The diagnosis was made of an immune checkpoint induced focal myocarditis, confirmed by MRI of the heart. The patient remained asymptomatic. No corticosteroids were given after extensive discussion with the cardiology department. Surprisingly a new MRI liver two months after initiating systemic therapy showed a significant shrinkage of tumor to a 5.5 cm diameter with central necrosis, indicating tumor response. After multidisciplinary discussion the patient was now considered a candidate for LTX. Seventeen months after diagnosis of HCC and eight months after discontinuation of atezolizumab/bevacizumab a LTX was performed. Pathology of the explant liver revealed a tumoral nodule of 5 x 2.7 x 2.6 cm but with just a 3 mm focus of viable residual tumor tissue. No oncologic problems nor organ rejection have occurred in the follow-up, but unfortunately the patient developed a heparin induced thrombocytopenia (HIT) syndrome two months after LTX, complicated by thrombosis of the inferior caval vein and subsequent an intracranial haemorrhage. Today, patient is alive and in a revalidation program.
Discussion: In this case atezolizumab/bevacizumab demonstrated a successful downstaging of HCC after failure of radioembolization and a LTX could be performed. This combination has been approved since 2020 as a new standard of care and has changed the field of systemic therapy for HCC. This case is remarkable given the impressive and durable tumour response despite only two cycles of systemic therapy and because of the early detection of immunotherapy induced myocarditis. Moreover, no organ rejection occurred following LTX, and very likely because of the intentional waiting time of more than six months between the last administration of immunotherapy and listing for LTX. Conclusion: The combination of atezolizumab/bevacizumab has the potential to downstage patients with HCC and liver transplantation after checkpoint inhibition treatment seems feasible in highly selected patients. Nevertheless, this type of systemic therapy may be associated with important side effects, warranting close follow-up and early intervention.

- C10 -

NEW ONSET INFLAMMATORY BOWEL DISEASE AFTER INITIATION OF ANTI-IL-17A TREATMENT. J. Geldof (1), M. Truyens (1), G. Dewitte (1), S. Akhayad (1), E. Glorieus (1), A. Hoorens (1), T. Lobaton (1) / [1] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology and Hepatology.

Case Report: Immune mediated inflammatory diseases (IMIDs) are a heterogenous group of inflammatory disorders of joint, skin and gut that share several pathological mechanisms. However, current treatment options are not effective for all IMIDs, and paradoxical occurrence of a new IMID in patients under biologic treatment has been described. Treatment with anti-IL-17a has been approved for ankylosing spondylitis (AS), psoriasis, and psoriatic arthritis, but was not found effective for the treatment of inflammatory bowel disease (IBD). This case study describes two patients who developed new-onset IBD after initiation of an IL-17a inhibitor. The first case concerns a 31-year-old man under 4-weekly injections of secukinumab for psoriasis vulgaris. He presented at the emergency department with abdominal pain, bloody diarrhoea and weight loss (6kg) since 3 weeks and blood analysis showed a high CRP (106.7mg/L). For 2 years, his psoriasis was being treated with secukinumab after previously failed PUVA therapy, ciclosporin, methotrexate and etanercept. A sigmoidoscopy confirmed an atypical patchy, mild, left-sided colitis. Histological features on biopsies were compatible with acute infectious-type colitis, immunohistochemistry and PCR for cytomegalovirus (CMV) and faecal cultures were negative. Initially the patient was treated with antibiotics, but no clinical or biochemical improvement was observed after

which systemic steroids were initiated. Some amelioration was noted but the diarrhoea persisted, the control endoscopy showed diffuse colitis with ulcerations and the biopsies now confirmed active chronic colitis. These findings were strongly suggestive for a new diagnosis of IBD type ulcerative colitis (UC). Infliximab was initiated which led to a rapid clinical and biochemical improvement. On repeated sigmoidoscopy around week 10 of therapy, complete endoscopic remission (endoscopic Mayo 0) was observed. However, 6 months later due to a psoriasis flare-up and infliximab-induced hepatitis and arthritis, infliximab was stopped and ustekinumab was started. Under treatment with ustekinumab a good evolution of all 4 IMIDs was seen. The second case concerns a 28-year-old woman diagnosed with AS 2 years prior. Initially she was treated with etanercept but due to loss of response subcutaneous ixekizumab 80mg 4-weekly was started together with a course of etoricoxib. However, soon after she developed severe diarrhoea, abdominal pain and 10kg of weight loss, requiring hospitalisation. Biochemical analyses revealed an elevated CRP (32.8 mg/L) and faecal calprotectin (386 mg/kg). Ileocolonoscopy revealed an erosive terminal ileitis, with ulcerations on the ileo-caecal valve, mild erythema in the sigmoid and some ulcerations in the ascending colon and the rectum. Histopathological analyses showed chronic ileitis with active inflammation and ulceration. Moreover, there was a diffuse colitis with active inflammation and cryptolytic granulomas. The endoscopical and histological image were suggestive of Crohn's disease (CD). A tapering course of oral budesonide (9mg) was started and etoricoxib and ixekizumab were immediately discontinued. After multidisciplinary discussion treatment with adalimumab (40mg, 2-weekly) was initiated. Initially, adalimumab had a good effect on both gastrointestinal and articular complaints. Based on recurrent articular symptoms after 6 months of treatment, adalimumab dosing was intensified to weekly administration. Elevated serum and mucosal concentrations of IL-17 have been described in patients with IBD, which led to the hypothesis that IL-17 inhibition might be effective for this indication. However, studies that assessed the effectiveness of anti-IL-17a treatment found a lack of efficacy and higher rates of disease worsening compared to placebo. Additionally, several cases of exacerbations or new onset of IBD during anti-IL-17a treatment have been reported. Nevertheless, the question remains whether the detection of new onset or exacerbation of IBD during anti-IL-17a treatment is actually due to the drug or rather an accidental observation as a consequence of the common association between different IMIDs. The incidence rates of IBD during anti-IL-17a treatment remain low and do not seem to exceed the general incidence rates of IBD in patients with other IMIDs. Therefore, the causal association between anti-IL-17a treatment and IBD development or deterioration remains doubtful. Either way, since secukinumab and ixekizumab are not effective for IBD one could therefore consider evaluating for subclinical IBD prior to treatment initiation.

BELGIAN SOCIETY FOR GASTROINTESTINAL ENDOSCOPY (BSGIE)

- G01 -

CAN WE EXTEND ESD INDICATION FOR CIRCUMFERENTIAL SUPERFICIAL ESOPHAGUS SQUAMOUS CELL CARCINOMA DEEPER THAN M2? M. Ayari (1), T. Moreels (2), E. Perez-Cuadrado-Robles (2), J. Chevaux (2), R. Altwegg (2), A. Taha (2), H. Dano (2), H. Piessevaux (3), P. Deprez (4) / [1] Hôpital des forces de sécurité intérieure de La Marsa, Marsa Safsaf La Marsa Tunis, Tunisia, Gastro-entérologie, [2] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Hépato-Gastro-Entérologie, [3] Cliniques universitaires St-Luc, UCLouvain, Brussels, Belgium, Hépato-Gastro-Entérologie, [4] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Gastro-entérologie.

Introduction: Although oesophageal location increases the difficulty of endoscopic treatment due to a narrower lumen and limited manoeuvrability of the scope especially for extended lesion, endoscopic submucosal dissection (ESD) is gradually turning into the treatment of choice for superficial esophageal neoplasia as a potentially curative treatment. Current guidelines (ESGE, JGES) recommend ESD for circumferential oesophageal squamous cell carcinoma (SCC) if clinically staged T1a-m1 /m2. Pre-therapeutic characterization and estimation of depth invasion can be challenging as requiring expertise, high-resolution endoscope with chromendoscopy for accurate pre-ESD staging evaluation.
Aim: The aim of our study was to evaluate the safety, results and long-term clinical outcomes of ESD for superficial circumferential oesophageal SCC.
Methods: We conducted a retrospective study from a prospectively collected database in a tertiary care endoscopy center including all consecutive patients treated by circumferential ESD for superficial oesophageal SCC between 2009 and 2022. Demographic, clinical, histological data, procedural characteristics and follow-up data were recorded. We investigated short-term outcomes including: en bloc, R0, curative resections, and adverse events in addition to long-term outcomes including overall survival (OS), cancer-specific survival (CSS), recurrence-free survival (RFS) and clinical course.
Results: From a cohort of 200 ESD for oesophageal SCC, 22 patients treated with circumferential resection were included with a mean age of 69 years ± 8 (range 55-88) and a sex ratio M/W =1. The mean lesion length, mucosal defect and procedure time were 48.6 mm ± 19.6 (range 20-90mm), 60 mm ± 14 (range 40-90mm) and 139 min ± 65, respectively. The en bloc resection, R0 and curative resections rates were 100%, 72.7% and 63.6%, respectively. At histologic examination, T1a m1–m2 tumours were found in 41% of cases. Regarding adverse effect, intra-procedural perforation occurred in three (13.63%) patients requiring endoscopic treatment by clips and delayed perforation occurred in one patient requiring intensive care unit admission for pneumomediastinum with good outcome. There were no bleeding complications. The 30 days mortality was of 4.5 % (N=1) due to infectious complications after ESD in an immunocompromised patient (cirrhosis and steroids intake). Sixteen patients (72.7%) had stricture prophylaxis: oral steroids alone (81%, N=13), oral + topical steroid (12.5%, N= 2), Topical steroid alone (6.5%, N=1). Among all patients, 68,2% (N=15) experienced oesophageal strictures with a mean delay of 95 (range 9-350) days. Strictures were managed by endoscopic balloon dilatation in most of cases (93.3%, N=14) associated to local injection of steroids in 7 patients and stenting in 2 patients, without adverse effects. One patient was treated by stenting alone. The mean number of endoscopic dilatations was 10 ± 8.1 (range 1-27). Regular diet was tolerated within a mean period of 201 days (range 1-639) after the first dilatation. The number of dilatations was significantly lower in patients treated by dilatation with local steroid injection versus dilation alone (mean 5.7 versus 14.3 respectively, p=0.04). Adjuvant treatment was indicated in 6 patients: radio-chemotherapy (N=5), radiotherapy (N=1) and immunotherapy (N=1). After a mean follow-up period of 40 ± 27 months, 3 (13.6%) patients had a neoplastic recurrence: metachronous (N=2), and pulmonary metastasis (N=1). The OS, CSS, RFS were 72.72%, 90.9%, 83.36% respectively with no significant difference between m1-m2 and m3-sm1 tumours. The 3-year overall survival rates of the m1/m2 and m3/sm1 were 90.9% and 81.81% respectively ($p>0.05$). Factors significantly associated with mortality in univariate analysis were moderately or poorly differentiated cancer ($p = 0.008$) and neoplastic recurrence ($p = 0.028$).
Conclusions: As to our knowledge, this is the first Belgium study investigating results of circumferential oesophageal SCC resection by ESD. For this indication, ESD, alone or associated to adjuvant treatment in non-curative resection, is an effective option treatment showing good security profile and favourable long-term outcomes even in m3-sm1 tumours. Strictures seems to be unavoidable but can be managed endoscopically with good functional results. Combining balloon dilation and steroid injection can allow lower number of dilatations. Further larger multicentric studies are warranted in order to confirm these findings for an optimized management.

- G02 -

SAFETY AND EFFICACY OF SALVAGE ENDOSCOPIC SUBMUCOSAL DISSECTION FOR BARRETT'S NEOPLASIA RECURRENCE AFTER RADIOFREQUENCY ABLATION. L. Mesureur (1), P. Deprez (2), R. Bisschops (3), R. Pouw (4), B. Weusten (5), M. Barret (6), P. Dewint (7), D. Tate (8), Ph. Leclercq (9), S. Seewald (10), F. Baldaque-Silva (11), F. Barbaro (12), M. Omae (12), M. Pioche (13), M. Bourke (14), R. Haidry (15), A. Lemmers (1) / [1] Erasme

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Introduction: Recurrence of dysplasia after radiofrequency ablation (RFA) treatment for Barrett's oesophagus is rare. Locally, RFA related fibrosis is important and might jeopardize further endoscopic resection. A niche for endoscopic resection using endoscopic submucosal dissection (ESD) focuses on fibrotic lesions with poor lifting as proposed by the ESGE guidelines. We aimed to review the experience of ESD for the removal of neoplasia recurrence after RFA.
Aim: The outcomes were the rate of complication of salvage ESD after RFA treatment (safety), the rate of complete resection (R0) and the rate of remission for neoplasia and / or intestinal metaplasia at the end of follow-up (efficacy). Computed incidence of the use of salvage ESD was reported.
Methods: We conducted a multicentric retrospective study, collecting data from patients in six Belgian, eight European and one Australian centers. We included all patients who achieved at least one RFA treatment for BE and had further oesophageal ESD for neoplasia recurrence after RFA.
Results: From April 2014 until June 2022, fifty-six patients with a mean age of 70 years were included. Before salvage ESD, the average number of RFA sessions was 2. Neoplasia recurrence occurred on average 25 months after the last RFA session. For salvage ESD, en-bloc resection was achieved in 89% and R0 resection was obtained in 76% of ESD done for HGD and in 49% of ESD done for ADC. Specimen analysis showed 37 ADC (66%), 17 HGD (30%) and 2 LGD (4%). Curative endoscopic resection for ADC (resection R0, no poor differentiation, no lymphovascular invasion and pT1a or pT1bsm1) was achieved in 46%. Immediate complications comprised 2 transmural perforations (4%) treated with stent or clip during the endoscopy. There was no delayed bleeding, 7 patients had strictures treated by dilatation with an average of 4.5 sessions. Among the 32 curative salvage ESD (17 ADC, 13 HGD and 2 LGD), 10 patients had additional treatment with RFA, APC or EMR. 3 patients required a second ESD for recurrence which resulted in remission for 2 of them. The last one still has ADC on biopsy, but surgery was contraindicated. Salvage ESD associated to initial curative specimen analysis is therefore associated to neoplasia remission for 97% of these patients after a follow-up of 21 months. 23 patients had non-curative ESD, 12 (21%) with local risk and 11 (20%) with high risk. From the local risk group (8 ADC and 4 HGD), 2 patients had RFA or APC treatment, 4 required a second ESD for recurrence which resulted in remission for two of them but one had still RFA sessions and the last one had adenocarcinoma and was treated by esophagectomy. One patient stopped his follow-up. From the high-risk group (11 ADC), 4 patients were treated by esophagectomy or chemoradiotherapy, one had RFA treatment, one required a second ESD for recurrence which resulted in remission. One patient had carcinoma recurrence during the endoscopic follow-up, but surgery was contraindicated because of his comorbidity. After a median of follow-up of 20 months, salvage ESD eventually combined with further ablation was associated to remission of neoplasia for 9 patients (75%) of the local risk group and 6 (55%) patients of the high-risk group. Despite salvage ESD, 4 patients from the high-risk group (36%) had to undergo surgery for the treatment of adenocarcinoma. Altogether, after a median follow-up time of 24 months, salvage ESD eventually associated to further endoscopic treatment was associated to neoplasia remission for 82% of the patients. Neoplasia remission reached 85 % and 80% of the patient with initial carcinoma and HGD on salvage ESD specimen, respectively. The median incidence of salvage ESD was 0.9 per 100 ESD for Barrett's oesophagus and 0.6 per 100 patients treated with RFA per center.
Conclusions: This multicenter retrospective study confirms that ESD performed by expert endoscopists is an efficient and safe treatment for recurrence of neoplasia after RFA treatment for Barrett's oesophagus and might therefore be proposed for selected cases after RFA in expert centers, with close endoscopic surveillance of the patients.

- G03 -

COMPARISON OF ESD AND EMR IN EARLY BARRETT'S NEOPLASIA. M. Noreillie (1), D. De Wulf (2), R. Bisschops (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [2] AZ Delta, Roeselare, Belgium, Gastroenterology.

Introduction: Current guidelines support endoscopic resection (ER) as first-line treatment in superficial Barrett's neoplasia. The choice between endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) remains controversial and western data are scarce.
Aim: We compared lesion characteristics, adverse events, clinical outcomes, and recurrence between both techniques.

Methods: A bicentric, retrospective analysis was performed of patients undergoing endoscopic resection of visible Barrett's lesions. Data were given for the histopathology, the en bloc and R0 resection rate. Rates of perforation, gastrointestinal bleeding, strictures, pre- and post-endoscopic diagnosis and recurrence were evaluated.
Results: 289 patients were included between February 2016 and May 2022. 282/289 underwent complete ER (204 EMR, 78 ESD). The en bloc resection (73.0 vs 94.9%, $p < 0.001$) and R0 resection rates (70.1 vs 83.3%, $p < 0.001$) were lower for EMR compared to ESD. Overall complication rates were low, without a significant difference between EMR and ESD (postprocedural bleeding: 4/204 (2.0%) in EMR and 1/78 (1.3%) in ESD, no perforations, strictures: 16/204 (7.8%) in EMR and 7/78 (9.0%) in ESD). Procedural time was longer in ESD (median time 63.7 minutes versus 29.7 minutes in EMR, $p < 0.001$), but lesion size for ESD was significantly larger than for EMR (median surface 8.48 cm^2 vs 2.36 cm^2 respectively, $p < 0.001$). Adjusted for the size, resection time per cm^2 of resected specimen showed no significant difference between ESD and EMR (respectively 10.1 and 6.7 min/cm^2, $p = 0.471$). Indications for additional surgery were lesions with high risk of lymph node metastasis, R1 resection for EAC and recurrences not amenable for ER. Surgery was more often needed after ESD (16/78, 20.5%) than EMR (11/204, 5.4%), in 10/16 ESD cases because of high-risk T1b lesions. The median follow-up time was 39 months (IQR 25-59). There were no significant differences in recurrence rates for HGD and EAC between both techniques after 1, 3 and 5 years.
Conclusions: The field of ESD expands and represents an alternative strategy that could be preferred to EMR in case of large or bulky lesions or when superficial submucosal invasion is suspected. Compared to EMR, it offers higher R0 resection and en bloc resection rates, with potentially better staging. Our data showed no differences in complication rates or resection time, when adjusted for size.

- G04 -

ENDOSCOPE TIP CONTROL – A SIMPLE, EX-VIVO MODEL WITH POTENTIAL FOR ENDOSCOPIST BENCHMARKING AND TRACKING OF PROGRESS OVER TIME. L. Debels (1), S. Smeets (1), P. Poortmans (1), V. Lala (1), C. Jorissen (1), L. Desomer (2), Research Team Endoscopy UZ Ghent (1), J. Anderson (3), R. Valori (3), D. Tate (1) / [1] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology and Hepatology, [2] AZ Delta, Roeselare, Belgium, Department of Gastroenterology and Hepatology, [3] Cheltenham General Hospital, United Kingdom, Department of Gastroenterology and Hepatology.

Introduction: Operator dexterity is recognised as a critical determinant of outcomes after surgery. No such recognition exists for the quality of endoscope tip manipulation (tip-control) and no objective measurement scale exists.
Aim: The aim of this study was to develop and validate a score for tip-control in an ex-vivo setting.
Methods: A web application containing a time score with clickable buttons to indicate correct and incorrect application of snare tip soft coagulation (STSC) was developed. The score was tested on a training model containing 4 shapes constructed from 1-4 identical circles (radius 1.4cm) connected at their mid-points drawn onto a single piece of cooked ham. Endoscopists with varied profiles consented to video recording of their timed complete application of STSC (=hits) to sequential circles using a gastroscope. Correct application was defined as any visualised diathermy application touching the marked lines. Median accuracy (=correct-hits/incorrect-hits) and correct hits per second (=speed) were determined by a single rater over the 4 recordings and stratified by shape and endoscopist demographic.
Results: 22 endoscopists (8 [36.4%] trainees, 14 [63.6%] consultants (of which 6 [27.3%] non-interventional and 8 [36.4%] interventional endoscopists)) participated. Participant median accuracy was 82.0% (IQR 17.5, 95%CI 77.0-85.0) and correct hits/second 0.141 (IQR 0.095, 95%CI 0.120-0.160). Accuracy strongly correlated with blinded rater opinion of the macroscopic ham appearance (correlation coefficient=0.78, P<.001). A scatter plot of endoscopist accuracy versus correct hits/second categorized generated 4 groups (accurate/inaccurate, fast/slow) (Figure 1). Interventional endoscopists were commonly fast and accurate (accuracy 88.0% [P=.001], correct hits 0.191/s [P=.04]) versus other participants. Non-interventional consultants had the lowest accuracy numerically and statistically similar tip-control to other participants (accuracy 69.0% [P=.15], correct hits 0.135/s [P=.97]) (inaccurate). Trainees had similar tip-accuracy to non-trainees but had lower correct hits/second (accuracy 73.6% [P=.25], correct hits 0.153/s [P=.03]) (slow). Endoscopists with >5 years' experience did not have better tip-control (accuracy 88.0% [P=.07], correct hits 0.132/s [P=.36]).
Conclusions: This is the first demonstration of an ex-vivo objective tool to assess the quality of endoscopic tip manipulation. Tip-control reliably stratifies endoscopists by important demographics including interventional profile, number of polypectomies performed and those performing difficult polypectomy but not years of endoscopy experience. If tip-control can be linked to performance it may provide an objective benchmark for endoscopy and interventional procedures, allowing tracking of progress over time.

- G05 -

THE ACCURACY OF SNARE TIP SOFT COAGULATION APPLIED TO THE MARGIN OF POST ENDOSCOPIC MUCOSAL RESECTION DEFECTS CORRELATES WITH ENDOSCOPIST POLYPECTOMY EXPERIENCE AND PROCEDURAL DIFFICULTY. L. Debels (1), S. Smeets (1), P. Poortmans (1), C. Jorissen (1), V. Lala (1), L. Desomer (2), R. Valori (3), J. Anderson (3), D. Tate (1) / [1] Ghent University Hospital, Ghent, Belgium, Department of

Gastroenterology and Hepatology, [2] AZ Delta, Roeselare, Belgium, Department of Gastroenterology and Hepatology, [3] Cheltenham General Hospital, , United Kingdom, Department of Gastroenterology and Hepatology.

Introduction: Operator dexterity is recognised as a critical determinant of outcomes after surgery. No objective metric exists for the quality of endoscope tip manipulation (tip-control).
Aim: We aimed to validate a previously described tip-control score in-vivo, using post endoscopic mucosal resection (EMR) snare tip soft coagulation (STSC) of the margin.
Methods: A web application containing a time score with clickable buttons was used to record correct and incorrect application (=hit) of STSC to the margin of a defect after piecemeal EMR. Correct hits were any visualised diathermy applications touching the defect margin. 2 blinded raters scored sequential videos of STSC performed by consenting endoscopists. Accuracy (=correct-hits/incorrect-hits) and correct hits/second (=speed) were determined. Results were stratified by polypectomy complexity (SMSA[+] score), difficulty of STSC application (independent movement of the colonic wall not explained by the movements of the endoscope = movement artefact] and experience of the endoscopist (expert vs fellow-in-training).
Results: 39 STSC procedures performed by 10 endoscopists (3 experts, 7 fellows) were rated. 12 (30.8%) polyps were SMSA 2 or 3, 3 (7.7%) were SMSA 4, and 24 (61.5%) were SMSA+. 24 (61.5%) STSC procedures were categorized as difficult. Median accuracy of STSC was 86.0% (IQR 19.5, 95%CI 77.0-91.0) and median correct hits/second was 0.175 (IQR 0.113, 95%CI 0.130-0.210). Accuracy strongly correlated with blinded rater impression of the tip-control demonstrated in the video (correlation coefficient=0.81, P<.001). Movement artefact significantly adversely impacted both overall accuracy (P=.06) and speed (P=.05). Increasing SMSA score adversely impacted overall accuracy (SMSA 4 vs SMSA+, P=.04), but not speed (P=.61). Fellows-in-training were significantly less accurate (76.5% vs 92.0%, P<.001) and slower (0.155 vs 0.202 hits/s, P=.02) versus experts in applying STSC. Movement artefact significantly impacted the performance of fellows (accuracy with artefact 68% vs 88%, P=.036, 0.151 vs 0.213 hits/s, P=.07) but not experts (P=.281 and P=.483). In procedures without movement artefact, performance of fellows and experts were similar (accuracy P=.106 and speed P=.148). In SMSA+ polyp observations with movement artefact trainees were significantly less accurate than experts (80.0% vs 92.0%, P=.045).
Conclusions: This is the first in-vivo description of a score for the quality Endoscopist tip manipulation. Endoscopist accuracy and correct hits/second were inversely related to trainee status, polypectomy difficulty and degree of movement artefact when applying STSC. The score ranges presented here could be used to benchmark endoscopists and fellows with respect to SMSA scores, guide progression through SMSA levels and correct tip-control scores for movement artefact due to patient breathing.

- G06 -

ENDOSCOPIC SUBMUCOSAL DISSECTION IS SAFE AND EFFECTIVE FOR LESIONS LOCATED AT THE ANORECTAL JUNCTION: ANALYSIS FROM TWO REFERRAL EUROPEAN CENTERS.

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Introduction: Endoscopic submucosal dissection (ESD) is well-established resection technique for colorectal superficial tumours. However, evidence of its efficacy in anorectal junctions is still scarce and its role in the treatment of anorectal junction (ARJ) lesions still remains to be determined.
Aim: With this study, we aimed to evaluate the feasibility, safety and efficacy of ESD for the resection of ARJ lesions (<20 mm from the dentate line), in comparison to more proximal rectal lesions.
Methods: We performed a retrospective analysis of prospectively collected data concerning all consecutive rectal ESD procedures performed in two European centers, from 2015 to 2021.
Results: A total of two hundred and fifty-two rectal lesions were included. Sixty (24%) were ARJ lesions and the remaining 192 (76%) were located proximally. Technical success was achieved in 248 procedures (98%), and its rate was similar in both locations (p=0.246). Most of the lesions presented high-grade dysplasia/ Tis adenocarcinoma (54%); 36 (15%) had submucosal adenocarcinoma, including 20 superficial (sm1) and 16 deeply invasive (>SM1) T1 cancers. We found no differences between ARJ and rectal lesions in regards to : en-bloc resection rate (100%vs96%, p=0.204), R0 resection rate (76%vs75%, p=0.531), curative resection rate (70%vs70%, p=0.920), procedures' median duration (120min vs 90min, p=0.072), ESD velocity (14vs12 mm2/min, p=0.415), histopathology result (p=0.053), and the need for surgery due to a non-curative ESD (5%vs3%, p=0.739). Also, there was no statistically significant difference in which concerns delayed bleeding (7%vs8%, p=0.709), perforation (0%vs5%, p=0.075) or the need for readmission (2%vs2%, p=0.939). Nevertheless, anorectal stenosis (5%vs0%, p=0.003) and anorectal pain (9%vs1%, p=0.002) were significantly more frequent in ARJ lesions.

Conclusions: ESD is a safe and efficient resection technique for the treatment of rectal lesions located in the anorectal junction.

- G07 -

RESIDUAL MALIGNANT CELLS ARE PRESENT IN THE ENDOSCOPE WORKING CHANNEL AND/OR BIOPSY FORCEPS IN ALMOST HALF OF THE CASES AFTER COLORECTAL CANCER ENDOSCOPIC BIOPSIES. P. Leclercq (1), S. Vansteenberge (1), O. Plomteux (1), N. Blétard (2), J. Radermacher (2), B. Bastens (1) / [1] Clinique Mont Legia - CHC Groupe Santé, Liège, Belgium, Gastroenterology, [2] Clinique Mont Legia - CHC Groupe Santé, Liège, Belgium, Pathology.

Introduction: ESGE guidelines suggest obtaining possible non-neoplastic biopsies before suspected malignant lesions to prevent the intraluminal spread of malignant disease. Nevertheless, very scarce data support this recommendation recently approved with a low level of evidence.
Aim: We checked for the possible presence of residual malignant cells in the endoscope working channel or on the biopsy forceps after endoscopic biopsies of colorectal adenocarcinoma.
Methods: At the end of 26 diagnostic colonoscopies with a colorectal cancer diagnosis (only sampled with biopsy forceps), as soon as the endoscope was removed, we shacked the empty biopsy forceps in a vial of 30 mL Cytolyt solution ("biopsy forceps sample"), then flushed the endoscope working channel with 20 mL of saline solution ("working channel sample") and then brushed the endoscope working channel with a cleaning brush which was then shaken in a vial of 30 mL Cytolyt solution ("brush sample"). After a "proof-of-concept" phase (Group A) of 10 cases where the three samples were pooled together for the cytological analysis, we screened 16 additional cases where the samples (Group B) were analysed separately to allow us to identify where the potential malignant cells were specifically found.
The cytological samples were stained with Papanicolaou stain. Then, Formalin-Fixed Paraffin-Embedded blocks were performed to get a slide stained in Haematoxylin-Eosin.
Results: Group A analysis showed the presence of malignant cells on a pooled analysis of cytologic samples in 7/10 cases. Group B analysis showed the presence of malignant cells in the "biopsy forceps sample" in 7/16 cases, in the "working channel sample" in 6/16 cases, and in the "brush sample" in 3/16 cases. At least one cytological sample was positive for malignant cells in 9/16 cases. The presence of malignant cells was positive in at least one sample in 62% overall group (A + B) and 43% for at least one working channel sample (flush or brush) in group B.
Conclusions: This study shows the presence of residual malignant cells in the endoscope working channel and/or biopsy forceps in almost half of the cases after colorectal cancer biopsies performed during a diagnostic colonoscopy. These preliminary results are of unknown clinical significance and could justify further studies.

- G08 -

ENDOSCOPIC DETECTION OF CANCER WITHIN COLORECTAL POLYPS BY YOUNG GI ENDOSCOPISTS: A PRE- AND POST-INTERVENTION ANALYSIS OF 680 INDIVIDUAL RESPONSES. P. Poortmans (1), L. Debels (2), J. Anderson (3), R. Valori (4), L. Desomer (5), D. Tate (2) / [1] UZ Brussel, Belgium, Gastroenterology and Hepatology, [2] Universitair ziekenhuis Gent, Belgium, Gastroenterology and Hepatology, [3] Cheltenham General Hospital, United Kingdom, Gastroenterology and Hepatology, [4] Gloucestershire Hospitals NHS Foundation Trust, United Kingdom, Gastroenterology and Hepatology, [5] AZ Delta, Roeselare, Belgium, Gastroenterology and Hepatology.

Introduction: Endoscopic imaging to assess the risk of cancer in colorectal polyps is the main tool to decide on their management. Inadequate assessment may lead to incorrect decision making (e.g. surgery for benign disease or piecemeal resection of a polyp containing cancer) and is associated with negative outcomes for patients and excessive healthcare costs.
Aim: The aim of this study was to assess if a short educational intervention can improve the ability of gastrointestinal endoscopists to accurately assess the presence of cancer in colorectal polyps.
Methods: We invited young gastrointestinal endoscopists (newly qualified consultants with <3 years independent practice and current trainees) to partake in a survey consisting of 20 standardized videos of ≥20mm non-pedunculated colon polyps presented in a random order. The participants were asked for their first impression on the presence of cancer within the displayed polyp. Subsequently, participants were invited to a 90-minute online educational intervention (gieqs.com/polyp-cancer). The intervention focused on the use of a structured online tool to detect cancer within polyps (gieqs.com/smi) based on i) the presence of a demarcated area to search for visible cancer and ii) 4 characteristics of polyps (size, granularity, location and Paris classification) to assess the risk for covert/hidden cancer. The course included 7 examples of polyps which were assessed using the above algorithm and allowed for interaction during the discussion of these examples. Finally, the participants completed a second survey containing the same 20 videos (no prior feedback given on histopathology) and were again asked for their first impression of the presence of cancer within these polyps. The responses were compared to blinded histopathologic data.

Results: A total of 680 responses were obtained from 17 participants who completed both surveys. Before the educational video accuracy for assessment of cancer within polyps was 50.3% (95% confidence interval (95% CI) 40.4-60.2%) with a sensitivity of 69.1% (95% CI 53.7-84.5%) and specificity of 45.6% (95% CI 35.8-55.3%). After the educational course, the accuracy, sensitivity and specificity all increased significantly to 69.7% (95% CI 64.8-74.6%) ($P < 0.001$), 88.2% (95% CI 76.3-100.1%) ($P = 0.043$) and 65.1% (95% CI 52.2-78.0%) ($P < 0.001$) respectively. The trainee group (N=13) had lower accuracy (46.9%, 95% CI 34.6-59.2%), sensitivity (65.4%, 95% CI 45.4-85.4%) and specificity (42.3%, 95% CI 30.6-54.0%) before the educational intervention when compared to the consultants (accuracy 61.2% (95% CI 43.6-78.9%), sensitivity 81.2% (95% CI 61.4-101.1%), specificity 56.2% (95% CI 31.9-80.6%)). After the educational intervention however, the trainee group's accuracy, sensitivity and specificity significantly increased to 69.6% (95% CI 63.9-75.3%) ($P < 0.001$), 90.4% (95% CI 82.7-98.0%) ($P = 0.036$) and 64.4% (95% CI 57.1-71.7%) ($P < 0.001$) respectively. The consultants' accuracy significantly increased to 70.0% (95% CI 52.8-87.2%) ($P = 0.035$); their sensitivity did not change, but a positive trend in specificity was noted (67.2%, 95% CI 46.9-87.7%) ($P = 0.102$). When compared to the trainee group, consultants had higher accuracy, sensitivity and specificity before but not after the educational intervention.
Conclusions: A short online educational intervention can significantly improve the ability of both qualified and trainee endoscopists to accurately assess and reliably exclude cancer in colorectal polyps. These results highlight the importance of developing and educating structured algorithms to optimize decision making in polypectomy and thereby prevent the negative patient outcomes associated with over- and underdetection of cancer in colorectal polyps.

- G09 -

CLINICAL VALIDATION OF A COMPUTER-AIDED DETECTION MODEL FOR COLORECTAL POLYP DETECTION (CAD-ARTIPOD) TRIAL USING A SECOND OBSERVER AND REAL-TIME UNBLINDING.
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Introduction: Computer-aided detection (CADe) improves colorectal polyp detection and needs to be clinically tested as an objective measure.
Aim: This trial aimed to validate a novel CADe system for colorectal polyp detection versus trained endoscopists in an innovative endoscopy blinded set-up with real-time unblinding by a second observer. This study design allows to assess the performances of both CADe and endoscopists.
Methods: The CAD-ARTIPOD trial is an investigator-initiated prospective multicenter trial conducted in 9 European centers. The CADe system is unique in design combining a convolutional neural network with a recurrent neural network for detection of colorectal polyps trained in all imaging modalities. Sample size analysis for superiority in polyp detection required 2048 polyps assuming a difference in sensitivity of 2% with endoscopic diagnosis as gold standard. All participating endoscopists (adenoma detection rate (ADR) 20-50%) were blinded to the CADe output. A trained second observer assessed and classified in real time the CADe output in (1) true positive, either detected or not detected by the endoscopist, (2) False negative or (3) clinically relevant or irrelevant false positive detection. The endoscopist was the gold standard for the primary endpoint (endoscopic lesion detection) and if a CADe detected polyp was not picked-up by the endoscopist, the endoscopist was unblinded for confirmation of the finding. All polyps detected and confirmed endoscopically were resected. Histological assessment was performed by two independent histopathologists.
Results: A total number of 2080 polyps were collected in 856 patients of which 1902 (91.0%) polyps were resected and 1549 (81.3.%) were histologically confirmed as hyperplastic polyp, adenoma or sessile serrated lesion. For the primary endpoint superiority was not reached between CADe and endoscopists with a sensitivity of 0.94 and 0.96, respectively (non-inferiority margin of 5%, $p = 0.0216$). The CADe system detected 3.7% extra polyps, missed by the endoscopist. False positive rate was 1.8/min and 37.2% of those were deemed as clinically relevant. With histology as diagnostic

standard, CADe outperformed the endoscopists with a sensitivity of 0.96 versus 0.95 (p=0.03) and showed an extra detection rate of 4.8%. Baseline polyp detection rate (PDR) increased from 0.47 to 0.70 during the trial (delta 0.48, OR 2.76 (95% CI: 2.26 – 3.37)). Similarly, ADR increased from 0.38 at baseline to 0.50 (delta 0.27, OR 1.52 (95% CI: 1.26; 1.85)).
Conclusions: This manufacturer independent CADe system used in an innovative and competitive study design demonstrated non-inferiority in comparison to endoscopists' polyp detection. However, with histology as gold standard, CADe outperformed endoscopists. Our study also shows that "watching over a shoulder" in itself leads to higher PDR and ADR.

- G10 -

DIGITAL SEDATION DOES NOT AFFECT CAECAL INTUBATION RATE DURING COLONOSCOPY AND CAN REDUCE DOSE OF PROPOFOL REQUIRED FOR INTRAVENOUS SEDATION: RESULTS OF A MONOCENTRIC RANDOMIZED CONTROLLED TRIAL. A. Pavlidi (1), L. Triki (1), J. Mortier (2), J. Devière (1), A. Lemmers (1), V. Huberty (1), C. Quoilin (3), T. Tuna (2), M. Arvanitakis (4), D. Blero (5) / [1] HUB Hôpital Erasme Brussels, Brussels, Belgium, Department of Gastroenterology, Digestive Oncology and Hepatopancreatology, [2] HUB Hôpital Erasme Brussels, Brussels, Belgium, Aneasthesiology Department, [3] Oncomfort SA, Wavre, Belgium, Scientific. Commission, [4] HUB Hôpital Erasme Brussels, Brussels, Belgium, Department of Gastroenterology, Digestive Oncology and Hepatopancreatology, [5] CHR, Namur, Belgium, Gastroenterology.

Introduction: Colonoscopy is still associated with physical and emotional discomfort requiring intravenous sedation (IVS). The downsides of IVS include intra- and post-procedural adverse events (AE), patient agitation, longer stay in different settings (procedure room, recovery room, day clinics…), as well as higher costs. Clinical hypnosis has shown pronounced effects on acute pain and anxiety reduction when delivered during medical procedures. Nevertheless, many obstacles hinder further implementation of this method. Digital sedation (DS) consists in using a three-dimensional, immersive virtual reality (VR) technology to guide the patient through similar steps as clinical hypnosis.
Aim: The primary outcome of this non inferiority trial was to demonstrate adequate colonoscopy performance (caecal intubation rate) in the experimental arm (DS). Secondary outcomes included the rate of rescue IVS in the experimental arm, as well as evaluation of pain, anxiety, comfort, and fatigue in the experimental arm (DS) compared to the control arm (IVS), preferred type of sedation for the patient, health care professionals (HCP) experience, additional performance measures related to colonoscopy and occurrence of AE.
Methods: Patients scheduled for screening or diagnostic colonoscopy with IVS were proposed for inclusion during the pre-procedural visit with the anesthesiologist. Exclusion criteria included active Inflammatory Bowel Disease, need for colon dilation, as well as auditory and/or visual limitations precluding the optimal use of DS. Patients were randomized (2:1 in favor of the experimental arm) either in the control (standard IVS with propofol) or the experimental group (DS using the Aqua© module of the Oncomfort device, with rescue IVS by propofol if needed).
Results: From 1/06/20 to 5/10/21, 93 patients were screened, and 90 patients included (IVS:30, DS:60). Baseline characteristics were similar, apart IVS patients being taller (respectively 168.2 cm vs 172.8 cm, $p = 0.02$). There was no difference regarding the primary outcome of caecal intubation rate (92.8 % in DS vs 100% in IVS, $p = 0.3$). The rescue sedation rate in the DS group was 63.6 % (38/60). Nevertheless, there was a significant decrease in total dose of propofol (mg/kg) per patient (1,15 mg/kg in the DS group and 4,41 mg/kg in IVS group, $p<0,00001$) and even in the subgroup of DS patients with IVS rescue (3,17 mg/kg in the DS group and 4,41 mg/kg in IVS group, $p=0,003$), as well as a shorter duration of sedation (70% for DS group, and 26.8% for DS with rescue sedation, as compared to IVS). Regarding patient experience, pain during colonoscopy was significantly higher in the DS group (3 vs 0, $p<0.0001$) and comfort was higher in the IVS group (10 vs 7, $p<0.0001$). In the DS group, 80% of patients would recommend DS to others. Regarding HCP experience, there was an overall lower evaluation for both anaesthesiologists (3 vs 5, $P < 0.0001$) and endoscopists (4 vs 5, $P < 0.0001$) in the DS group. There was no difference regarding other colonoscopy performance measures such as adenoma detection rate or AE. Finally, duration of procedure was comparable in the two groups, but patients in the DS arm stayed longer in the procedure room (46.5 min vs 41.5 min, $p = 0.03$) but less in the recovery room (39.5 min vs 54 min, $p = 0.02$), with no difference in overall stay.
Conclusions: This randomized controlled trial showed that patients could successfully undergo colonoscopy with the help of DS with similar outcomes compared to IVS regarding performance measures. Even if more than half the patients under DS required rescue IVS, the total dose of propofol was lower than in the IVS arm.

- G11 -

ENDOSCOPIC ULTRASOUND-DIRECTED GASTROJEJUNOSTOMY TO TREAT GASTRIC OUTLET OBSTRUCTION: WHICH TECHNIQUE IS THE BEST? L. Monino (1), E. Perez-Cuadrado-Robles (2), J. Gonzalez (3), C. Snauwaert (4), M. Gasmi (3), A. Alric (2), S. Ouazzani (3), P. Deprez (1), G. Rahmi (2), C. Cellier (2), T. Moreels (1), M. Barthet (3) / [1] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Gastroenterology, [2]

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Introduction: Gastric outlet obstruction (GOO) of malignant or benign origin represents a clinical challenge with different therapeutic options: endoscopic duodenal stenting or surgical gastrojejunostomy. Recently endoscopic ultrasound-directed gastrojejunostomy (EUS-GJ) was developed as a minimally invasive technique with very good technical and clinical outcome. The technique relies on the EUS-directed creation of a gastrojejunal fistula using a large size lumen-apposing metal stent (LAMS) (15*10 mm or 20*10 mm). However, the technique of EUS-GJ is not standardized and different variations of the procedure have been described. In the 'direct method' the target jejunal limb is punctured directly from within the gastric lumen. In the 'assisted method' the target jejunal limb is filled with liquid in order to improve its identification and close approximity to the gastric wall before puncture. In addition, the 'free-hand method' uses no guidewire, whereas in the 'guide-wire method' a wire is inserted into the target jejunal limb. No direct comparison of the techniques is currently available.
Aim: Comparison of the free-hand assisted method (WEST technique) and the guide-wire direct method to create a gastrojejunostomy using EUS-GJ to treat GOO.
Methods: Retrospective multicenter study in 4 European tertiary centers including all patients who underwent EUS-GJ to treat GOO from 2017 ot 2022. Technical success was defined as the creation of an EUS-GJ without rescue or redo technique. The primary objective was to compare technical success and complication rate between the free-hand assisted method and the guide-wire direct method. Secondary objective was the clinical outcome.
Results: A total of 85 patients were included (54% females, mean age 66±10 years). In 69 patients (81%) GOO was caused by malignancy. The free-hand assisted WEST technique was used in 41 patients and the guide-wire direct technique in 30. Technical success rate was 73% for the guide-wire direct technique as compared to 95% for the free-hand assisted technique (HR 6.9; IC 95% [1.23 ;72.12], p=0.014). Technical success rates with additional rescue procedures increased to 93% and 98% respectively. Perprocedure complications were LAMS misdeployment in 6 patients (20%) in the guide-wire direct group and in 2 patients (5%) in the free-hand assisted group. Postprocedure complication rate was 26%, which were mostly minor (AGREE grade II). Procedure-related mortality was 3.5% (3 patients). There were more complications in the guide-wire direct group (47%) as compared to the free-hand assisted group (15%) (HR 4.96; IC [1.472 ; 18.93] ; p=0.007). Total clinical success rate 1 month after the EUS-GJ was 96% (73/76), with 89% (25/28) in the guide-wire direct group versus 98% (39/40) in the free-hand assisted group.
Conclusions: The free-hand assisted (WEST) technique combines a free-hand puncture of the prefilled target jejunal limb. This technique seems to be the most efficient and safe technique to perform EUS-GJ in patients with both malignant or benign GOO, in comparison with the guide-wire direct technique which combines the insertion of a guide-wire into the target limb without prefilling.

- G12 -

IDENTIFICATION OF 6 KEY FEATURES OF COLORECTAL POLYPS INCREASES THE SENSITIVITY OF CANCER DETECTION AND ABILITY TO DISCRIMINATE DEEP SUBMUCOSAL INVASION - THE BASIS OF THE BLINK (FIRST) IMPRESSION?

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Introduction: Decision making regarding the presence of cancer in colorectal polyps is poorly performed by endoscopists. Prior study demonstrates that Blink (first) impression has a high sensitivity amongst experienced endoscopists for polyp cancer. Differentiation between superficially and deeply submucosally invasive polyp-cancer remains difficult even for experts despite being critical for appropriate treatment stratification and subsequent patient outcomes.
Aim: We aimed to determine whether identification of 6 endoscopic features of polyp cancer can increase the sensitivity of cancer detection and endoscopist ability to differentiate deep submucosal invasive cancer (SMI).
Methods: An online survey was created containing 20 overview images of colorectal polyps (1 image/polyp). Images (randomized) were shown before, and again after a 2-minute educational video (the intervention) which introduced the six macroscopic (Blink) features of deep submucosal invasion - 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 the six Blink features were present. Responses were analysed relative to histopathology (no versus superficial [<1000µm] versus deep [>1000µm] submucosal invasion).
Results: 7/20 polyps shown contained cancer histologically (3 superficial, 4 deep submucosal invasion). 191 participants completed 3,755 observations (123 (64.4%) gastroenterologists, 22(11.5%) surgeons the remainder trainees). 108 (56.5%) had performed >1000 colonoscopies, 109 (57.1%) had performed > 50 endoscopic mucosal resections. The overall sensitivity of Blink impression (vs histopathology) increased after the educational intervention (0.67 [95%CI

0.65-0.70] pre versus 0.88 [95%CI 0.86-0.90] post [P<.001] but overall specificity decreased (0.69 [95%CI 0.67-0.71] pre versus 0.55 [95%CI 0.53-0.57] post [P<.001]). Surgeons had lowest sensitivity (0.59 [95%CI 0.51-0.66]) increasing significantly (P<0.001) after the intervention. Trainees achieved the greatest incremental gain in sensitivity after the intervention (+0.23, P<.001) at the cost of specificity (-0.18 P=.001). Participant reported mean number of Blink features correlated significantly with expert opinion (correlation coefficient 0.73, p<.001), with the histological presence of cancer (no cancer=1.1 versus cancer=2.2, p<.001) and with the histological depth of SMI (none=1.1, versus superficial invasion=2.0 [p =0.04], versus deep invasion=2.3 [p=0.003], superficial versus deep [p=0.409]). Per polyp, participants' Blink impression (pre-education) was significantly associated with the number of reported features post intervention in all except for 3 polyps all of which contained >3 features of SMI.
Conclusions: Significant improvement in the sensitivity of Blink (first) impression for cancer detection in colorectal polyps can be achieved by a structured approach amongst a mixed population of endoscopists. A standard set of 6 'Blink' features can be reliably identified and the number identified correlates with presence and degree of submucosal invasion. Adoption of this approach could minimise delays to correct treatment for patients and remove the need for extensive experience to use Blink impression.

- G13 -

OUTCOMES OF MINOR VERSUS MAJOR PAPILLA RENDEZ-VOUS FOR EUS-GUIDED PANCREATIC DUCT DRAINAGE. M. Bronswijk (1), D. Persyn (1), H. van Malenstein (1), W. Laleman (1), S. Van der Merwe (1) / [1] University Hospitals Leuven, Belgium, Gastroenterology and Hepatology.

Introduction: Retrograde endoscopic therapy for symptomatic chronic pancreatitis is often hampered by the ability to access the pancreatic duct (PD). EUS-guided pancreatic duct drainage (EUS-PD) has been suggested to overcome these limitations, with a preference for rendez-vous versus pancreaticogastrostomy. In some cases, large stones or extensive fibrosis in the pancreatic head may preclude a rendez-vous through the major papilla, leading to preferential guidewire advancement through the minor papilla. Little comparative evidence is available on the outcomes of EUS-PD rendez-vous through the minor papilla.
Aim: Our aim was therefore to evaluate the outcomes of minor papilla EUS-PD rendez-vous and compare these with standard major papilla rendez-vous.
Methods: This is a tertiary single-center retrospective analysis of all consecutive EUS-PD procedures performed for symptomatic chronic pancreatitis from 2015 to April 2022. Successful EUS-PD rendez-vous cases were included and minor and major papilla procedures were compared. Exclusion criteria were: 1) post-chirurgical anatomy, 2) placement of an EUS-guided pancreatogastrostomy, 3) follow-up <90 days and 4) technical failures (inability to achieve intraductal access and/or guidewire advancement). All EUS interventions were performed under general anaesthesia, using either a 19G- or 22G-needle with a 0.025-inch or 0.018-inch guidewire respectively. Primary outcomes were clinical success, defined as resolution of pain/symptoms, and adverse events using the ASGE lexicon for adverse event grading.
Results: Sixty procedures were identified, of which 27 were excluded due to post-chirurgical anatomy (n=9), technical failure (n=9) or placement of a pancreatogastrostomy (n=11). In total, 33 patients were included in the final analysis (66.6% male, mean age 56.1 ±14.8 years, 54.6% active smokers). EUS-PD was performed following failed ERCP in all patients. In 21 out of 33 patients (63.6%), minor papilla rendez-vous was used. Clinical success was achieved in 81.0% vs. 58.3% in the major papilla group (p=0.230). The overall incidence of AE was similar in both groups (9 [42.9%] vs. 4 [33.3%] events, p=0.719), with a comparable distribution in severe (0 [0%] vs. 1 [8.3%] events, p=0.364) and moderate AE (1 [4.8%] vs. 2 [16.6%] events, p=0.538). No fatal AE occurred. In the minor papilla rendez-vous group, 1 moderate AE occurred, consisting of post-procedural pancreatitis with pseudocyst formation, for which eventually EUS-guided drainage was performed. The remainder of complications were mild (n=8) and characterized by immediate post-interventional pain without signs of pancreatitis. These were successfully treated with opioid analgesia in all cases. A trend towards a higher incidence of mild AE was however seen when comparing both groups (8 [38.1%] vs. 1 [8.3%] events, p=0.107). Two moderate AE occurred in the major papilla group, one of which was due to formation of a small, infected collection, which was successfully treated with antibiotics, whereas the other event consisted of an inward migration of a plastic stent into a pre-existing collection in the pancreatic head. At reintervention, LAMS placement was performed, followed by immediate through-the-LAMS stent extraction. In the same group, one patient suffered a severe AE with an episode of upper gastrointestinal bleeding for which the patient underwent prolonged observation and endoscopic re-evaluation, resolving following conservative measures. No significant differences were detected regarding recurrent pancreatitis rates when comparing minor and major papilla rendez-vous (28.6% vs. 25.0%, p=1.000).
Conclusions: For patients with symptomatic chronic pancreatitis, EUS-PD with minor papilla rendez-vous attained similar results when compared to major papilla rendez-vous. These data suggest that in cases where standard major papilla rendez-vous is not possible or accidental minor papilla cannulation is achieved, pancreatic duct drainage through the minor papilla can be considered as equally effective.

- G14 -

MOTORIZED SPIRAL ENTEROSCOPY: NEW INDICATIONS. H. Colin (1), L. Monino (1), H. Piessevaux (1), T. Moreels (1) / [1] UCL Saint Luc, Brussels, Belgium, Gastroenterology.

Introduction: The motorized spiral enteroscope PowerSpiral (PSF-1) is a newly developed axial view video-enteroscope of about 1680mm long (standard colonoscope length) with an external diameter of 11.5mm. It is combined with the PowerSpiral tube (DPST-1), a 31mm wide overtube with soft spiral-shaped fins which is mounted onto the PSF-1 and the forward and backward rotations are activated by foot pedals. It was developed to overcome shortcomings of other types of device-assisted enteroscopy, like balloon-assisted enteroscopy. Initially, its use was not recommended in patients with surgically altered anatomy of the gastrointestinal tract.
Aim: The aim of this work is to characterize new indications for the use of the PSF-1 and to extend its field of possibilities.
Methods: Monocentric retrospective descriptive study on 75 patients who underwent enteroscopy using PSF-1 January 2020 and April 2022, excluding patients included in the Olympus SAMISEN studies. Patient's characteristics, indications for enteroscopy, and procedure-related data were extracted from the medical electronic file and technical success rate and adverse event rate were calculated.
Results: A total of 75 patients underwent PSF-1 enteroscopy. The cohort comprised 41 men (54.7%) and 34 women (45.3%). Mean patient age was 60.8 years (range 19-94). Among all procedures 51% were antegrade procedures and 21% were retrograde procedures in patients with normal gastrointestinal anatomy with conventional enteroscopy indications (chronic anemia and overt gastrointestinal bleeding in most cases). The remaining 28% of the patients underwent PSF-1 procedures for secondary less conventional indications: n=6 (29%) underwent retrograde enteroscopy after previous incomplete conventional colonoscopy, n=8 (38%) underwent antegrade enteroscopy after Roux-en-Y gastric bypass (RYGB) and n=7 (33%) underwent enteroscopy-assisted ERCP after surgically altered anatomy. In this group of secondary indications, technical success was achieved in 90.5% of the patients. Failure to complete the procedure was encountered in 2 patients (9.5%): n=1 inability to introduce the PSF-1 through a strictured colo-anal anastomosis in the group of incomplete colonoscopy, n=1 inability to cross the Roux-en-Y anastomosis in the RYGB group. Minor secondary adverse events occurred in 13/75 (17%) with no mortality registered. Most of them were superficial mucosal lacerations in the upper oesophagus (AGREE grade I). Two patients underwent CT scan due to abdominal pain after the enteroscopy, showing air bubbles around the small bowel suspect for intestinal perforation, n=1 after retrograde enteroscopy and n=1 after enteroscopy-assisted ERCP. Both patients completely recovered after medical treatment (AGREE grade II).
Conclusions: Despite the initial warning from the manufacturer not to use PSF-1 in patients with surgically altered anatomy, this retrospective study demonstrates its usefulness for secondary less conventional indications in daily practice. PSF-1 is useful to complete colonoscopy after incomplete conventional colonoscopy due to dolichocolon, it can be used to reach the excluded stomach after Roux-en-Y gastric bypass and to perform ERCP in patients with surgically altered anatomy. Technical success rates are high for these secondary indications with an acceptable minor adverse event rate.

- G15 -

HYBRID EMR AS A SALVAGE TECHNIQUE DURING COLONIC EMR. S. Van Langendonck (1), N. Van Heddegem (1), J. Bekaert (2), K. Rasquin (1), P. Dewint (1) / [1] Maria Middelares Ziekenhuis, Gent, Belgium, Gastro-enterologie, [2] UZ Brussel, Belgium, Gastro-enterologie.

Introduction: Endoscopic resection of colorectal polyps has drastically reduced the need for surgery for this pathology, with endoscopic mucosal resection (EMR) being the standard modality. Endoscopic submucosal dissection (ESD) is getting more widely spread, though apart from the rectum, this technique is still mostly reserved for cases where superficial submucosal cancer is predicted and in which en-bloc and curative resection is paramount. Nevertheless, prior studies show that in up to 10% of EMR a complete resection during the initial procedure cannot be achieved, necessitating additional surgery or other salvage therapy. With increasing knowledge of ESD techniques we've started adopting hybrid EMR in these cases, where partial submucosal dissection is undertaken with the snare tip for lesions where conventional EMR failed during the procedure due to inability of the snare to grab (a residual fragment of) the polyp often, though not always, due to severe fibrosis.
Aim: To investigate whether supplementing conventional EMR with hybrid EMR when the first fails, is safe and reduces the need for additional surgery or salvage therapy in a second session.
Methods: All EMR and hybrid EMR procedures, together with patient and polyp characteristics, performed in a non-academic Belgian center between September 2015 and February 2022 were retrospectively collected and analysed. For safety parameters we looked at rate of adverse events (all complications, clinically relevant complications (AGREE classification >1), severe complications (AGREE classification >3b) and perforations). Finally, we looked at outcome parameters, namely en-bloc resection rate, primary successful resection rate, defined as technically successful resection during first procedure without need of immediate surgery, recurrence rate and need for surgery due to endoscopically not manageable recurrence. All data was analysed in Statistical Package for the Social Sciences (SPSS, v28). Data between the groups was compared using crosstabs and significance tested with a Chi square test.

Results: In total 301 procedures were performed of which 20 with hybrid technique. Most notable characteristics are hybrid EMR having more lesion >30mm (30% vs 23,8%), more NICE 3 lesions (18,2% vs 12,3%) and more superficial submucosal colorectal cancer (10,5% vs 5%), none of which were statistically different between the groups. The en-bloc resection rate was 25% for EMR and 15% for hybrid EMR, with a recurrence rate of respectively 11,7% and 5,0% and need for surgery due to non-endoscopically manageable recurrence of respectively 1,4% and 0%, all statistically not significant. The adverse event rate was 7,9% for EMR and 10% for hybrid; a clinically relevant complication rate of 6,0% vs 10%; a severe complication rate of 1,8% vs 0% and a perforation rate of 0,7% vs 0%, again none of which were statistically different between the groups. Finally, we see that 4,1% of our EMR were primary unsuccessful, compared to 10% of or hybrid EMR (p ns), or a total of 6,9% of our procedures, which would have been statistically significantly higher at 10,8% (p=0,005) if we hadn't embarked on hybrid EMR.
Conclusions: Embarking on Hybrid EMR during the same procedure in cases where conventional EMR was technically unsuccessful, seems to be a highly effective salvage method, with a numerically lower recurrence rate than conventional EMR and with a significantly reduced need of postprocedural surgery or endoscopic salvage therapy. Moreover, in experienced hands, this technique does not lead to a significantly higher complication rate.

- G16 -

ENDOSCOPIC TREATMENT OF IATROGENIC PERFORATION AT THE UPPER OESOPHAGEAL SPHINCTER AFTER REMOVAL OF AN ULTRAFLEX STENT. L. Monino (1), P. Deprez (1), T. Moreels (1) / [1] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Gastroenterology.

Video Abstract: This videocase shows the endoscopic closure of an iatrogenic perforation after Ultraflex stent removal in the proximal oesophagus just below the upper oesophageal sphincter. A 65-year-old female patient with a history of breast cancer and small cell lungcarcinoma, underwent a circumferential endoscopic mucosal dissection (ESD) of a squamous cell carcinoma in the middle third of the oesophagus with signs of radiation oesophagitis. One day after the ESD procedure she developed subcutaneous emphysema due to a perforation at the ESD site. A partially covered Ultraflex stent was placed covering the perforation. Pathological analysis confirmed R0 resection of a well-differentiated pT1am2 squamous cell carcinoma. One month later, the stent was removed by inversion and the initial perforation at the ESD site was closed. However, one day later she developed again subcutaneous emphysema and repeat endoscopy confirmed the presence of a 5 mm wide fistula where the proximal flange of the Ultraflex stent had been at 2 cm below the upper oesophageal sphincter. The fistula was fully closed using a 9 mm Ovesco over-the-scope clip placed just beneath the upper oesophageal sphincter. The patient recovered well and follow-up endoscopy confirmed complete healing of the ESD site without tumor recurrence and complete fistula closure at the level of the upper oesophageal sphincter.

- G17 -

ENDOSCOPIC VACUUM THERAPY OF ANASTOMOTIC LEAKS COMPLICATING COLORECTAL SURGERY. L. Monino (1), J. Gonzalez (2), R. Bachmann (3), D. Leonard (3), A. Kartheuser (3), S. Berdah (4), C. Remue (3), M. Gasmi (2), M. Barthet (2), T. Moreels (5) / [1] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, Gastroenterology, [2] Assistance Publique des hôpitaux de Marseille, Hôpital Nord, Marseille, France, Gastroenterology, [3] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Digestive surgery, [4] Assistance Publique des hôpitaux de Marseille, Hôpital Nord, Marseille, France, Digestive surgery, [5] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Gastroenterology.

Introduction: Postoperative anastomotic leak is a common complication (4-15%) of colorectal surgery leading to increased morbidity and mortality and often requiring redo or rescue surgery with perineal amputation and permanent colostoma. Endoscopic vacuum therapy (EVT) is an innovative technique based on continuous negative pressure application in the peri-anastomotic collection, leading to improved drainage and closure of the cavity.
Aim: Study of the faesibility and efficacy of EVT to treat anastomotic leaks after colorectal surgery.
Methods: Retrospective study in 2 university centers including all patients referred for endoscopic treatment of large anastomotic leaks with pelvic collections after colorectal surgery from 2015 to 2022. EVT was indicated to treat chronic pelvic sepsis before rescue surgery or to treat an anastomotic leak with pelvic cavity. All procedures were performed under general anaesthesia under endoscopic and fluoroscopic control. A gastroscope was introduced through the anal canal up to the rectal anastomosis and into the para-anastomotic cavity in order to clean it by removing purulent debris. The EndoSponge overtube was then inserted into the cavity and the EVT sponge attached to a catheter was positioned through the overtube into the cavity. A continuous negative pressure pump was connected to the catheter with the sponge in order to aspirate pus and to induce tissue repair. The sponge needed to be replaced every 3 to 4 days using the same endoscopic procedure. When the volume of the cavity was reduced to less than 10 mm, the sponge was positioned into the colorectal lumen in close apposition to the remaining anastomotic fistula until complete closure. Technical success was defined as complete closure of the anastomotic leak and cavity. Clinical success was defined as successful closure and absence of recurrence 1 month after ending the endoscopic treatment as confirmed by CT scan.

Results: A total of 30 patients underwent rectal EVT and in 27 after complicated colorectal surgery. In 4 patients EVT was indicated to treat chronic pelvic sepsis before rescue surgery (perineal amputation). A total of 23 patients were included to analyse the use of EVT to treat anastomotic leaks after colorectal surgery (30% females, mean age 65±9 years). Technical success with complete closure was achieved in 19/23 patients (83%), among them 16/23 (70%) without additional surgical intervention. In total 160 endoscopic procedures were performed in 23 patients with a mean of 7 sponge replacements per patient. Mean procedural time was 17 minutes. In 9/23 patients (40%) patients were treated on an ambulatory base. Total complication rate of the EVT treatment was 22% (6/27 patients) without procedure-related mortality. Complications were minor (AGREE grade II n=5) or moderate (AGREE grade IIIb n=1). Clinical success rate was 70% (16/23) without recurrence of pelvic collections 1 month after ending the endoscopic EVT treatment.
Conclusions: EVT is feasible and efficient to treat anastomotic leaks with pelvic collections after colorectal surgery in the majority (70%) of patients, without further surgical intervention. It can also lead to a healthier pelvic environment to improve redo surgery outcome. Complete treatment requires a mean of 7 sponge exchanges, which can also be performed on an ambulatory base.

- G18 -

QUALITY MONITORING OF GASTROSCOPY AND COLONOSCOPY BY MEANS OF ESGE QIC-APP. F. Wouters (1), R. Bisschops (2), P. Roelandt (2) / [1] KUL - University of Leuven, Leuven, Belgium, Faculteit Geneeskunde, [2] KUL - University of Leuven, Leuven, Belgium, TARGID, UZ Leuven.

Introduction: Over the last decade, quality in endoscopy was promoted by ESGE and different quality indicators (PMs) with target standards were defined. Quality measuring is important but sometimes difficult to perform when electronic systems are lacking. The ESGE QIC-app was developed, and it was suggested that a snapshot of 300 procedures is sufficient to audit endoscopy practice on the level of the endoscopy unit.
Aim: We wanted to assess the feasibility of the QIC-app to audit retrospectively gastroscopy and colonoscopy practice in a tertiary center. As a secondary goal, we wanted to calculate the administrative cost for this quality assessment in the absence of automated systems.
Methods: 300 gastroscopies and 300 colonoscopies, performed between 01-05-2021 and 01-07-2021, were retrieved from the electronic patient record system from the hospital. Since therapeutic procedures are excluded for most PMs, we only selected diagnostic procedures. They were then divided so that each physician (N= 11) was equally represented in the study. These procedures were entered into the ESGE QIC-app. The ESGE secretary provided an Excel file from the data entered through the QIC app that was used for analysis. The time spent distributing procedures, entering and analysing data was closely monitored to get an estimate of the budget needed for quality measurement.
Results: It is clear there is a better performance for colonoscopy in comparison to gastroscopy. For gastroscopy, it is evident that data required for PM measurement that are automatically entered in the report (eg Prague classification, Forrest classification) score better than features that are not automatically entered in the report (eg time of procedure). Indeed, patients always receive written instructions for fastening with their invitation, however this is not systematically included in the report or patient file, hence not auditable. In the period studied, the data in the series of colonoscopy met the various indicators to the following extent: 100% timeslot per colonoscopy, 83% adequate bowel preparation, 98% indication for colonoscopy, 74% photo documented caecal intubation rate, an adenoma detection rate (ADR) of 30.3% and an polyp detection rate (PDR) of 51%, 95% documented withdrawal time (WT), 93.4% appropriate technique for polypectomy, 40% tattooing of the resection site, polyp retrieval rate (PRR) of 100%, advanced imaging assessment in 100%, 81% adequate description of polyp morphology, 0% complication rate, 0% patient experience, post-polypectomy surveillance of 89.5%. The results for gastroscopy data were as follows: 43% adequate pre-procedure instructions, 39.3% documentation of procedure time, 14% accurate photo documentation, 77.8% use of standardized terminology, 79.2% adequate inspection time of Barrett's oesophagus, 72% use of Seattle protocol in Barrett's surveillance, 83% MAPS guidelines, 0% complication rate, 0% patient experience and 100% registry of patients with Barrett's oesophagus. The time spent on this study was 53 hours and 25 minutes. Calculated at an hourly wage of €20-30, this would amount to about €1,068.33 to €1,602.50 in costs.
Conclusions: The ESGE QIC-app allows monitoring quality of an endoscopy unit with a minimal financial and logistic effort. It allows to provide a quality snapshot of a unit, and guide quality improvement initiatives. In addition, it can provide to ESGE data to assess which PMs are less important if the prevalence is low in an audit sample. It is also clear that the lack of structured reporting hampers quality auditing or reaching quality standards. In the end, if you cannot measure it, it does not mean that things do not happen. We found that, on parameters that automatically appear in a report, overall scores are clearly better. Accordingly, targets were met more frequently, which thus underlines the importance of standardized structured reporting systems.

- G19 -

THE CASE "EMR VERSUS ESD IN THE COLON". P. Corens (1), S. Van Langendonck (1), N. Van Heddegem (1), J. Bekaert (2), K. Rasquin (1), P. Dewint (1) / [1] AZ Maria Middelares, Ghent, Belgium, Gastroenterology and Hepatology, [2] University hospitals Brussel, Jette, Belgium, Gastroenterology and Hepatology.

Introduction: The case on resection technique in oesophagus and stomach is settled: in general, ESD has become the preferred and most reliable technique in removing neoplastic lesions. However, the case for the colon is more complicated. Whereas ESD is associated with a higher en bloc and R0 resection rate and a more reliable histopathological analysis, the arguments against ESD are in essence the higher complication risk and associated higher risk for urgent surgery.
Aim: To comparatively investigate key performance measures and safety profile of EMR and ESD in colonic lesions.
Methods: All patients who underwent colorectal EMR or ESD between September 2015 and February 2022 in a non-academic Belgian center were retrospectively collected and analysed. Patient and polyp characterstics were registered. Outcome parameters were en bloc resection, R0 resection, adverse events (all complications, clinically relevant complications (AGREE classification > 1), severe complications (AGREE classification > 3b) and surgery due to adverse events) and local recurrence rate. Statistical analysis was performed with SPSS, v28. Comparative analysis was performed using cross tabulations.
Results: In 448 patients (mean age 72y; 58.2 % males), a total of 448 endoscopic colorectal resections were performed of which 281 (62.6 %) with EMR and 168 (37.4 %) with ESD. In patients who underwent endoscopic resection, 24.3% (n=109/448) were on Acetylsalicylic acid, 3.1% (14/448) were on P2Y12 antagonists and 9.8% (44/448) on anticoagulants. Endoscopic imaging revealed NICE I (10.4% vs. 0%), NICE II (77.4% vs. 71.6%) and NICE III-lesions (12.3% vs. 28.4%) (p = .002). Large polyps (defined as > 30 mm in size) were more present in the ESD group (49.7% vs 23.8%) (p <.001) En-bloc and R0 resection rates were significantly lower in the EMR group as compared to the ESD group (25% vs. 80.8%; p < .001) and (38.8% vs 73.8%; p < .001) respectively. Local recurrence rate was significantly higher in the EMR group (11.7% vs. 0.6%; p < .001}, necessitated surgical resection in 4/281 (1.4%) patients vs. 0% in ESD group) (p=ns) EMR resulted in a lower overall complication rate (7.9% vs 14.9%; p = .019), however no statistically significant differences were observed regarding clinically relevant complications (6% vs. 10.1%; p ns) or severe complications (1.8% vs. 1.8%; p ns). Similar early and delayed post-procedural bleeding rates were found between the EMR and ESD group (early bleeding 1.4 vs 1.8%; delayed bleeding 4.6 vs. 3.6%; p ns) No patients required surgical intervention as a consequence of an adverse event.
Conclusions: Our data confirm that in an expert center, ESD has the well described benefits of high en bloc and R0 resection rates together with a lower recurrence rate as compared to EMR. Furthermore, we showed that in this setting, ESD is a safe technique not leading to a higher rate of clinically significant complications. This suggests that in expert centers the decision to choose ESD over EMR for selected colonic lesions can be advocated.

- G20 -

HOW FEASIBLE AND SAFE IS COLONIC ESD IN A NON-ACADEMIC SETTING IN BELGIUM? P. Leclercq (1), J. Zeevaert (2), O. Plomteux (1), S. Van Langendonck (3), R. Bisschops (4), P. Dewint (3) / [1] Clinique Mont Légia - CHC Groupe Santé, Liège, Belgium, Gastroenterology, [2] CHR Verviers, Verviers, Belgium, Gastroenterology, [3] AZ Maria Middelares, Ghent, Belgium, Gastroenterology, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology.

Introduction: Even though colonic ESD is common practice in Japan since many years, allowing higher rate of en-bloc and R0 resection (>90%), conflicting results are coming from Western countries. More recently, several multicenter French studies have shown promising results, especially in context of structured training, supervision, and traction strategy.
Aim: We aimed to evaluate the outcome of colonic ESD in 3 Belgian non-academic centers, with extensive experience in ESD.
Methods: We retrospectively analyzed data from all consecutive colonic ESD from a common prospectively maintained database, in three non-academic Belgian centers, realized between September 2019 and September 2022. Rectal ESD were excluded from the analysis.
Results: 73 colonic ESD were performed in three centers by five operators (2019-20: n=11; 2020-21: n=8; 2021-22: n=54). The mean age of the patients was 69.3 years. The mean size of the lesions was 47.6mm, granular-type LST in 66% of the cases. Lesions localizations were sigmoid: 31, left: 8, splenic flexure: 1, transverse: 7, hepatic flexure: 2, right: 11, caecum: 10, ileo-cecal valvula: 3. The mean duration time was 93.4 min (7-240) with a mean speed of 18 mm2/min. Double-clip traction with rubber-band strategy was used in 59% of the cases. The en-bloc, R0 and curative resection rate were 97%, 90% and 89%, respectively. The perforation rate was 2.7% (2/73), all managed endoscopically. Six patients (8.2%) required secondary surgery: because of complete failure of endoscopic resection (2/73) or for unfavourable histological reasons (4/73). Delayed bleeding occurred in 3 cases (4.1%). The mean hospitalization duration was 1.1 days. Final specimen histology was SSA in 1.4%, LGD adenoma in 46.5%, HGD adenoma in 32.9%, intramucosal adenocarcinoma in 6.8%, sm1 adenocarcinoma in 6.8%, >sm1 adenocarcinoma in 5.5%.
Conclusions: This retrospective multicenter Belgian study shows that colonic ESD is safe and reproducible, with results in terms of en-bloc, R0, curative resection rate, speed and complication rate comparable with those of large Japanese and French teams.

- G21 -

PERFORMANCE OF NOVICES IN ENDOSCOPIC SUBMUCOSAL DISSECTION STARTING DIRECTLY IN HUMANS UNDER DIRECT SUPERVISION OF AN EXPERT ENDOSCOPIST. J. Bekaert (1), S. Van Langendonck (2), N. Van Heddegem (2), C. De Bie (3), S. Gossé (4), M. Aerts (5), P. Dewint (2) / [1] Maria Middelares Ziekenhuis, Gent, Belgium, Department of Gastroenterology and Hepatology, [2] Maria Middelares Ziekenhuis, Gent, Belgium, Department of Gastroenterology and Hepatology, [3] AZ Klina, Brasschaat, Belgium, Department of Gastroenterology and Hepatology, [4] OLV Aalst, Aalst, Belgium, Department of Gastroenterology and Hepatology, [5] UZ Brussel, Jette, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Endoscopic submucosal dissection (ESD) was first described more than 30 years ago in Japan and is now widely practiced throughout Europe. ESD enables an en-bloc resection permitting an optimal histopathological assessment and reduction of recurrence but is associated with a higher complication rate compared to Endoscopic Mucosal Resection (EMR). The technique needs a very high level of expertise and is associated with a long learning curve and a set of prerequisites before starting the training.
Aim: Recently the ESGE curriculum guideline on training in ESD was published, in which an extensive experience in animal models is advised before continuing on to humans. However, the evidence on which this recommendation is based, is rather limited. In this retrospective study we evaluate the performance of novices in ESD during their one-year training period. The novices had none or very limited prior experience in animal models.
Methods: All ESD procedures performed by an expert endoscopist or one of the 3 novices in a single non-academic center from September 2015 until February 2022 were collected. An ESD in which a novice was involved, was defined as a supervised ESD (sESD) as direct supervision by an expert endoscopist with continuous feedback was guaranteed. The expert ensured a smooth and safe process of the procedure, with taking over only if needed. Outcome parameters were technical success, en-bloc and R0 resection rate, rate of adverse events (all complications, clinically relevant complications (AGREE classification > 1), severe complications (AGREE classification > 3b) and surgery due to adverse events) and recurrence. Additionally, patient characteristics (age, gender and relevant medication use) were registered along with lesion characteristics (location; Paris Classification, NICE, size). All data were analyzed with Statistical Package for the Social Sciences (SPSS, v28). Confounding factors were tested with multivariate analysis. Data between the groups was compared using crosstabs and significance tested with Chi square tests.
Results: In total 250 ESD were included; of which 124 sESD (49,6%), performed by a novice endoscopist under supervision. Patient characteristics show 61,9% males in the ESD group and 75,8% in the sESD group, average age 73,9 vs 69,5 years, 26,2% vs 22,6% respectively on acetylsalicylic acid, 3,2% vs 4,8% on P2Y12 receptor antagonists, 9,5% vs 11,3% on anticoagulants and 2,4% vs 1,6% on combination therapy, 1,6% vs 0,8% on chronic oral steroids, 53,2% vs 50,0% lesions >30mm, 5,6% vs 6,5% esophagus, 18,3% vs 13,7% Barrett, 2,4% vs 7,3% stomach, 12,7% vs 14,5% left colon, 36,5% vs 19,4% right colon and 24,6% vs 37,1% rectum. There were no statistically significant differences. Technical success rate for ESD and sESD was respectively 82,5% and 74,2%% (p ns); en-bloc resection rate was 88,0% vs 84,7% (p ns); R0 resection rate was 75,4% vs 75,0% (p ns); R0 resection rate for completed ESD was 80,2% vs 83,2% (p ns); all adverse events 19,0% vs 8,9% (p=0,028); clinically relevant complications 12,7% vs 6,5% (p ns); severe complications 3,2% vs 0,8% (p ns); perforations 4,8% vs 2,4% (p ns) and 3,2% vs 0% needing surgery due to complications (p ns). Recurrence rate was 4,8% for ESD and 1,6% for sESD (p ns). In 2 cases (1,6%) vs 0 (0%) (p ns) respectively, there was a need for additional surgery both in Barrett patients with carcinomatous recurrence, one who had initially declined surgery for a T1sm3 and one T1sm1. On multivariate analysis, NICE was found to be a predicting factor for technical success, R0 resection and recurrence, whereas all other patient and polyp characteristics were not.
Conclusions: This retrospective analysis demonstrates that learning ESD in humans without extensive prior animal model training is feasible, on the condition that continuous supervision by an expert is provided.

- G22 -

SMALL BOWEL POLYPECTOMY IN PEUTZ-JEGHERS SYNDROME: COMPARISON OF ENDOSCOPES AND RESECTION TECHNIQUES. T. Moreels (1), A. Donati (2), L. Monino (3), H. Piessevaux (3) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Hépato-Gastroentérologie, [2] CHU-UCL-Namur site Godinne, Yvoir, Belgium, Hépato-Gastroentérologie, [3] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Hépato-Gastroentérologie.

Introduction: Peutz-Jeghers syndrome (PJS) is a rare autosomal dominant genetic disorder originating from a mutation in the STK11 gene on chromosome 19. It is characterized by the development of hamartomatous polyps throughout the gastrointestinal tract from early age on. Since PJS polyps have the potential of becoming malignant, endoscopic resection of large polyps is advocated. However, the majority of PJS polyps originating in the small bowel (beyond Treitz' angulus) lead to subobstruction and small bowel invagination before malignant growth. In comparison to gastric, duodenal and colonic PJS polyps, small bowel PJS polyp resection may be more challenging because they are difficult to reach and the risk of perforation is considerable.

Aim: Evaluation of small bowel polypectomy procedures in a cohort of PJS patients with special interest in the type of endoscope and the polypectomy techniques used.
Methods: Retrospective analysis of a cohort of PJS patients who underwent small bowel polypectomy between 2014 and 2022. All patients were referred for therapeutic enteroscopy with polypectomy based on wireless videocapsule findings and/or MRI enterography findings. The endoscopic approach (antegrade vs retrograde) was decided upon based on previous diagnostic findings. All enteroscopy procedures were performed under general anaesthesia with endotracheal intubation, CO2 insufflation and with fluoroscopy control.
Results: A total of 13 PJS patients (10 females) aged 37±5 years (range 16-82) underwent 29 enteroscopy procedures in order to perform polypectomy in the small bowel. Prior to enteroscopy n=6 patients (46%) underwent surgical small bowel resection during childhood because of intestinal invagination with obstruction. The following endoscopes were used: pediatric colonoscope PCF n=3 (10%), single-balloon enteroscope SBE n=19 (66%) and motorized spiral enteroscope MSE n=7 (24%) (only intact small bowel). Antegrade enteroscopy was chosen in n=19 procedures (66%), retrograde in n=9 (31%) and peroperative enteroscopy n=1 (3%). The targeted polyps were reached in 67% using PCF, in 63% using SBE and 88% using MSE (with 2 antegrade panenteroscopy procedures reaching the caecum) (Chi square p=0.206). Small polyps (<2 cm Paris lp and lsp) were resected using hot snare polypectomy, medium size pedunculated polyps (2-3 cm Paris lp) were resected using a hot snare after placement of 1 or more hemostatic clips onto the stalk, giant pedunculated polyps (>3 cm Paris lp) were strangulated using an EndoLoop and left in place after confirmation of ischemia, and giant sessile polyps (>3 cm Paris lsp) were tattooed for future surgical resection. Using this approach, no adverse events occurred during therapeutic enteroscopy.
Conclusions: Treatment of small bowel PJS polyps is challenging but can safely be performed when taking into account their location in the small bowel and their anatomical characteristics. Polyps located deep into the small bowel can better be reached using the motorized spiral enteroscope. Giant pedunculated polyps can be strangulated and left in place using EndoLoops, and giant sessile polyps are best removed surgically. The use of the motorized spiral enteroscope in PJS patients with a history of intestinal resection remains to be elucidated.

- G23 -

ERCP IN PATIENTS WITH DIFFERENT TYPES OF TOTAL AND PARTIAL GASTRECTOMY. F. Fortunati (1), L. Monino (1), P. Deprez (1), H. Piessevaux (1), T. Moreels (2) / [1] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Hépato-Gastroentérologie, [2] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Hépato-Gastroentérologie.

Introduction: Endoscopic retrograde cholangiopancreatoscopy (ERCP) is the first-line treatment for the most part of pancreaticobiliary diseases, with a success rate of more than 95% in patients with normal anatomy. However, ERCP in patients with surgically altered anatomy is more challenging leading to lower success rates and higher complication rates.
Aim: In the present study, we analyzed ERCP procedures in patients with previous gastric surgery: total gastrectomy Roux-en-Y, partial gastrectomy Roux-en-Y, Billroth II gastrectomy, sleeve gastrectomy, duodenal switch and gastrojejunostomy (excluding Billroth I, Whipple's duodenopancreatectomy, Roux-en-Y gastric bypass). Outcomes were: technical success rate per patient by type of surgery and according to the type of endoscope used, complication rate and ERCP indications.
Methods: Monocentric retrospective analysis of a prospective cohort. All patients with a history of gastric surgery with an intact Vater's papilla who underwent ERCP between 2014 and 2022 were included. Data were collected from computerized medical records and the pharmacy databank of the hospital.
Results: 104 ERCP procedures were performed in 74 patients. Male/female ratio was 51/23 (69% vs 31%) with a mean age of 66±2 years and 69±3 years respectively. The proportions of surgery included 50% total gastrectomy Roux-en-Y, 16% partial gastrectomy Roux-en-Y, 19% Billroth II, 1% duodenal switch, 7% gastrojejunostomy and 7% sleeve gastrectomy. ERCP indications were mainly biliary: common bile duct stones (61%), biliary stricture (30%), postoperative bile leak (4%) and 5% for chronic calcifying pancreatitis. Overall technical success rate per patient was 57/74 (77%), with 17 patients needing alternative approaches like percutaneous biliary drainage, EUS-guided drainage, shock-wave lithotripsy or surgery. Technical failure was mainly encountered in the Roux-en-Y total (10/17 failures) or partial (4/17 failures) gastrectomy patients, representing a technical success rate after Roux-en-Y total gastrectomy of 73% and 67% after Roux-en-Y partial gastrectomy. Technical success rate after Billroth II and sleeve gastrectomy were 100%. All ERCP procedures performed in patients with Roux-en-Y total or partial gastrectomy were performed using a long or a short single-balloon enteroscope, whereas in patients with a sleeve gastrectomy conventional duodenoscopes were used. Billroth II patients all underwent technically successful ERCP using either a duodenoscope (57%), a single-balloon enteroscope (36%) or a pediatric colonoscope (7%). Overall complication rate was 8/104 procedures (8%) with mainly mild complications and without procedure-related mortality.
Conclusions: ERCP in patients with surgically altered anatomy is challenging, especially after Roux-en-Y total or partial gastrectomy with significantly lower technical success rates as compared to Billroth II or sleeve gastrectomy. Despite the lower technical success rate, complication rates are low and ERCP in patients with surgically altered anatomy is considered safe. Technical success rates in Billroth II patients is independent of the type of endoscope used (duodenoscope vs single-balloon enteroscope).

- G24 -

EFFICACY AND SAFETY OF G-POEM IN MANAGEMENT OF PATIENTS WITH REFRACTORY GASTROPARESIS: ABOUT 10 CASES. P. Kisoka (1), F. Wuestenberghs (2), E. Akpokavie (1), G. Burnet (1), N. de Suray (1), M. Del Natale (1), H. Hassaini (1), Z. Issa (1), C. Leu (3), S. Negrin Dastis (1), A. Sibille (1), P. Warzee (1) / [1] Grand Hopital de Charleroi, Charleroi, Belgium, Gastroenterology, [2] Centre Hospitalier Universitaire Mont-Godinne, Belgium, Gastroenterology, [3] Centre Hopitalier Epicura Baudour, , Belgium, Gastroenterology.

Introduction: Gastroparesis is a chronic disorder characterized by delayed gastric emptying in the absence of a mechanical obstruction. Management of patients with gastroparesis is challenging. Gastric peroral endoscopic myotomy (G-POEM) has been recently described as a new minimally invasive procedure with promising clinical results in patients with refractory gastroparesis.
Aim: We aimed to assess the short- and long-term efficacy and the safety of G-POEM for the treatment of refractory gastroparesis in secondary care.
Methods: We performed a retrospective analysis on patients from 2 centers (Grand Hôpital de Charleroi and Epicura) who underwent G-POEM between July 2019 and May 2022 for severe refractory gastroparesis. All patients were admitted to the hospital on the day of the procedure. G-POEM was performed under general anesthesia with a CO2 insufflator and a triangle knife (Olympus) by a single operator and included four principal steps: (1) submucosal injection followed by mucosal incision of the greater curvature 4–5 cm proximal to the pylorus, (2) creation of a submucosal tunnel towards the pyloric ring, (3) a complete pyloromyotomy extended to the distal antrum (10-15 mm long), (4) closure of the incision with endoscopic clips. Gastric emptying scintigraphy and GCIS score were performed before and 2 months after the procedure. Patients were then followed-up by phone call and the last GCSI score available was used for analysis. Data were analysed using GraphPad Prism 9 version 9.4.1 (681) for Windows® 64-bit (GraphPad Software Inc., San Diego, CA, USA, www.graphpad.com). All results were expressed by mean +/- standard deviation. Quantitative data were compared using a non-parametric paired t-test, the Wilcoxon matched-pairs signed rank test, whereas multiple groups comparisons were performed using Friedman test with Dunn's multiple comparison post-test to compare all pairs of columns, both with 95% confidence intervals. The correlation between variations of the GCSI and the half-emptying time was determined using the nonparametric Spearman correlation coefficient. A one-tailed p-value < 0.05 was considered statistically significant.
Results: A total of 10 gastroparetic patients (5 idiopathic, 3 postsurgical and 2 diabetic; 90% female; mean age of 57.1 +/- 16.3 yo) were treated by G-POEM. Median follow-up was 14.2 (5-28) months. Technical success was 100%. The procedure was associated with variations in the GCSI score ($p = 0.0091$). The mean GCSI score 2 months after the procedure was improved compared to baseline (1.99 +/- 1.38 vs. 3.49 +/- 1.13 points, $p = 0.016$) but the improvement was no longer significant in the longer term (mean GCSI at the end of follow-up: 2.51 +/- 1.41, $p > 0.05$). Mean gastric half-emptying time decreased significantly after G-POEM compared to baseline (116.8 +/- 56.6 vs. 167.3 +/- 60.7 min, $p = 0.027$). Variations in the GCSI score and in the gastric half-emptying time 2 months after the procedure were not correlated ($r = -0.4788$, $p = 0.083$). All patients were discharged the day after the procedure. There were no adverse events nor mortality.
Conclusions: G-POEM is safe and effective in the short-term in refractory gastroparesis in secondary care patients. Our study has several limitations however (retrospective, limited number of patients, no control group). Further studies are needed to confirm our results and identify predictive factors of response in the long-term before the procedure being used in routine care.

- G25 -

EUS-GUIDED DRAINAGE OF NON-SURGICAL PELVIC ABSCESSES USING SMALL SIZE LUMEN-APPOSING METAL STENTS L. Monino (1), R. Bachmann (2), M. Denis (3), D. Leonard (2), C. Remue (2), A. Kartheuser (2), T. Moreels (3) / [1] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, Gastroenterology, [2] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Digestive surgery, [3] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Gastroenterology.

Introduction: Pelvic abscesses of non-surgical origin are difficult to treat. Initial therapy consists of antibiotics and drainage of the abscess. Percutaneous drainage is not always possible due to interposition of pelvic organs or intestinal limbs. Transanal surgical drainage requires blind puncture of the abscess through the rectal wall. Endoscopic-ultrasound pelvic abscess drainage (EUS-PAD) is a valuable alternative to the percutaneous and surgical approach. The use of lumen-apposing metal stents (LAMS) might be superior to plastic pigtail stents to optimise transrectal drainage. Little is known about the efficacy of small size LAMS to drain pelvic abscesses of non-surgical origin.
Aim: To evaluate the feasibility and efficacy of small size LAMS to drain pelvic abscesses of non-surgical origin.
Methods: Retrospective analysis of a prospective cohort of patients who underwent EUS-PAD using small size LAMS (6*8 mm and 10*10 mm). EUS-PAD was indicated for patients unfit for surgical drainage and when the abscess was not percutaneously accessible.

Results: Five patients (4 men, 36-83 years) underwent EUS-PAD using small size LAMS (6*8 mm n=2 ; 10*10 mm n=3). None of the patients had a protective ileostomy since all abscesses were of non-surgical origin: diverticular abscess (n=2), perianal abscess (n=2) and pararectal abscess in Crohn's disease (n=1). EUS-PAD was performed using the HotAxios stents with the free-hand technique (n=3) or over the guide-wire after puncture of the abscess using a 19 G needle (n=2). Mean procedure time was 35 minutes with a 100% technical success rate. One LAMS was misdeployed and placed correctly using a rescue technique during the same procedure. Clinical success rate was 80% since 1 LAMS needed to be removed on day 2 because of severe anal pain. All LAMS were endoscopically removed after 2 weeks and replaced by a double pigtail stent in 2 patients. All 4 out of 5 patients with clinical success recovered well without pelvic abscess recurrence.
Conclusions: EUS-PAD using small size LAMS seems feasible and safe to treat pelvic abscesses of non-surgical origin in patients without protective ileostomy in whom surgical or percutaneous drainage is not possible. Small size LAMS can even be used in the distal rectum.

- G26 -

STER OF A SYMPTOMATIC ESOPHAGEAL LEIOMYOMA. M. Noreillie (1), L. Desomer (1), D. De Wulf (1) / [1] AZ Delta, Roeselare, Belgium, MDL.

Video Abstract:
Background: Surgery has long been the primary approach for resection of tumors arising from the esophageal muscularis propria. Nowadays endoscopic treatment by Submucosal Tunneling Endoscopic Resection (STER) is the treatment of choice for these lesions.
Case: We describe a case of a healthy 58-year-old male with dysphagia for solid food for a 4 months period. endoscopy, endoscopic ultrasound, video fluoroscopy and CT scan showed a 25 mm lesion arising from the esophageal muscularis propria. The lesion at 30 cm from the incisors was located close to the left atrium/pulmonary veins.
Methods: The resection is done with a Olympus GIF-HQ190 endoscope with a single-use straight distal attachment cap for ESD using a Triangle Tip Electrosurgical knife (Olympus). After prophylactic Cephalosporin administration we started with a longitudinal mucosal incision 4 centimeters proximal to the lesion after submucosal lifting with blue stained Geloplasma followed by creating a submucosal tunnel. The tunneling was finished when the complete leiomyoma was isolated and the normal circular internal muscle layer was visible around the lesion. In the next step we performed a circular incision of the complete muscularis propria around the leiomyoma. Special attention with a carefully traction on the triangle tip knife was needed to avoid heat damage of the left atrium and pulmonary vein. The tumor could be removed with a swirlnet (Olympus) and the mucosal defect closed with resolution clips (Boston Scientific). The patient recovered well and could be discharged the next day after a swallow X-ray excluding mucosal leakage. No early nor late complications occurred.
Conclusion: STER resection of a symptomatic oesophageal leiomyoma is feasible and safe and is associated with minimal comorbidity.

- G27 -

TRANSGASTRIC CIRCUMFERENTIAL ESD FOR ESOPHAGUS SCC. L. Triki (1), P. Eisendrath (1), F. Charara (2), I. El Nakadi (2), A. Bucalau (1), S. Belkhir (1), A. Hendlisz (3), A. Digonnet (4), L. Verset (5), J. Van Laethem (1), J. Devière (1), A. Lemmers (1) / [1] Erasme Hospital, Brussels, Belgium, Gastroenterology, [2] Erasme Hospital, Brussels, Belgium, Digestive surgery, [3] CUB Institut Jules Bordet, Brussels, Belgium, Gastroenterology, [4] Erasme Hospital, Brussels, Belgium, Cervicofacial surgery, [5] CUB Institut Jules Bordet, Brussels, Belgium, Anatomopathology.

Video Abstract: A 64-year-old patient is followed for remission of a pyriform sinus SCC treated by laryngectomy and radiotherapy A PETCT uptake a suspiscious lesion in the esophagus. Due to severe post-radic trismus it wasn't possible to introduce an adult gastroscope, 5Fr biopsies were obtained using a nasogastroscope revealing an esophageal adenocarcinoma. Decision to create access to the lesion a retro to the retro to the esophagus by creating a surgical large gastrostomy (ch32). With an adult HD gastroscope (GIF-EZ-1500) : the lesion was 6cm long on 85% of the circumference with features typical of squamous cell carcinoma (IIb+IIa, IPCL mostly B1, small part B3 on the nodule). We resected the lesion en-bloc circumferentially by the tunneling ESD technique. The extraction of 60x50mm specimen was performed under the protection of a surgical plastic bag to avoid cancer cell seeding to the abdominal wall. The large gastrostomy tube was kept for 4 weeks after the procedure to secure endoscopic access in case of complication. Pathological analysis revealed a 18x17mm foci of mucoepidermoid carcinoma infiltrating the submucosa (pT1sm2) on 713microns on an in-situ SCC. Margins were free of tumoral cells (HM, VM0), with no lymphovascular invasion. After MDT discussion, adjuvant radiotherapy was discussed with the oncologic team. In conclusion, superficial neoplastic lesion assessment needs a HD adult gastroscope. A retrograde approach to the oesophagus via a surgical gastrostomy is possible and allows to get access for assessment and resection by ESD of the superficial carcinoma.

- G28 -

COMPLETE ENDOSCOPIC RESECTION OF A 4CM OESOPHAGEAL LEIOMYOMA USING UNDERWATER SUBMUCOSAL TUNNELING ENDOSCOPIC RESECTION. D. Tate (1) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology.

Video Abstract: A 47-year-old patient presenting with dysphagia had a suspected leiomyoma detected in the mid-oesophagus at gastroscopy and endoscopic ultrasound. The patient consented to endoscopic resection of the abnormality. A submucosal tunneling endoscopic resection (STER) procedure was planned. In the submucosal plane a large leiomyoma was detected but due to difficulties with access (likely related to the size of the lesion) the resection was switched to an underwater approach with a water exchange device mounted on the endoscope. This allowed complete resection, removal of the specimen from the oesophagus and closure of the perforation. The patient recovered fully after the procedure and their dysphagia resolved. No recurrence of leiomyoma has been detected to current 1 year follow up.

- G29 -

GASTRIC BULB ENDOSCOPIC SUBMUCOSAL DISSECTION - A NOT SO HAZARDOUS TECHNIQUE. M. Figueiredo Ferreira (1), J. Aoun (1), P. Eisendrath (1), A. Lemmers (2) / [1] CHU Saint-Pierre, Brussels, Belgium, Gastroenterology, [2] Erasme Hospital, Brussels, Belgium, Gastroenterology.

Video Abstract: Grade 1 non-functional non-ampullary duodenal neuroendocrine neoplasms (NEN) of < 20mm have a low risk of metastasis, and removal by local excision is advised. Various endoscopic techniques may be applied, as long as an en-bloc R0 resection is achieved. Endoscopic submucosal dissection (ESD) has a high R0 resection rate, but it is often associated with great technical complexity. The aim of this video case is to describe some useful techniques and devices that can turn ESD into a less hazardous and more accessible technique in this context. We report the case of a 73-year-old man, who presented a gastric bulb grade 1 NEN (uT1N0 at endoscopic ultrasound and with no distant metastasis at OctreoPET). In order to have a higher stability of the scope, we filled the lumen with physiological serum (saline immersion technique). This also allowed for a better visualization of all the margins of the lesion, that “floated” within the surrounding clear liquid. We then injected a methylene blue/glycerol solution in the submucosa, to raise a mucosal bleb and create the space for a safe mucosal cut. The rest of the procedure was performed using a dual knife. A peri-procedural haemorrhage occurred, but the bleeding spot was easily identified using the red dichromatic imaging (RDI) and quickly treated with a bipolar haemostatic forceps. A R0 en-bloc resection of the G1 NEN (20 mm) was then achieved. This case illustrates practical and efficient ways to overcome duodenal ESD difficulties and make it more widely accessible and performant, with lesser risks of complications.

- G30 -

ENDOSCOPIC RESECTION OF GIANT DUODENAL LESIONS: EXPANDING INDICATIONS WITH A SERIES OF 5 CASES N. Pizarro-Vega (1), R. Garcés-Duran (1), H. Dano (2), N. Yahagi (3), P. Deprez (1) / [1] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Hepato-gastroenterology Dpt Clin, [2] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Pathology Department, [3] Keio University School of Medicine, Tokyo, Japan, Division of Research and Development for Minimally Invasive Treatment, Cancer Center.

Video Abstract: Duodenum lesions may progress to invasive carcinoma, and resection is therefore recommended. The location in the duodenum makes endoscopic resection difficult because of the increased risk of perforation, bleeding, and pancreatitis when the papillas are involved. However, thanks to advances in endoscopic techniques, more and more duodenal polyps are being resected in a minimally invasive way. We present 5 cases of “giant” duodenal lesions removed endoscopically from June to September 2022 in 4 W and 1 M aged 33-75 years, ranging in size from 40 to 70mm in length. They were pedunculated in 1 case and sessile or flat in 4. One involved the major papilla. None showed endoscopic signs of deep invasion. Resection was performed by piecemeal EMR in 2 cases, ESD in 2 others and EMR-ESD hybrid in the last patient. Complete resection was achieved in all 5. Haemostasis and closure of defect was attempted in all 5, by placement of endoclips, OVESCO (in 2), endoscopic suturing (in 1). PuraStat was applied in 3 pts. Histologically, the pedunculated lesion was found to be unaltered duodenal mucosa with erosive changes at its apex, 4 were adenovillous tumours all showing high-grade dysplasia with foci of carcinoma in situ in 2 of them. The absence of deep infiltration was demonstrated in all cases. There were no immediate complications. At 6 months follow-up no recurrence has been seen. These cases demonstrate the usefulness of advanced endoscopic management, including various techniques of hemostasis and defect closure, in giant duodenal lesions.

- G31 -

ESD RESECTION OF A GIANT LIPOMATOUS LESION AT THE UES LEVEL. M. Noreillie (1), P. Sinonquel (2), P. Nafteux (3), R. Bisschops (1), D. De Wulf (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] KUL - University of Leuven, Leuven, Belgium, Department of Translational Research in Gastrointestinal Diseases (TARGID), [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Thoracic Surgery.

Video Abstract:
Background: Tumors at the level of the upper esophageal sphincter (UES) are difficult to manage and must be discussed with thoracic surgeons, ENT and GI endoscopist. We demonstrate an ESD resection of a giant lipoma at this level.
Case: We describe a case of a 62-year-old man, having a respiratory arrest at the end of a diagnostic gastroscopy for dysphagia. A large pendulated tumor from the UES level prolapsed before the vocal trachea origin. During CPR and intubation, the lesion could be pushed back into the esophagus. CT scan showed a large lesion (2 x 3 x 7 cm) lesion suggestive for lipoma.
Methods: We decided to resect the giant lipoma with ESD. The lesion originated at the backside of the arytenoids and continued into the proximal oesophagus. The ESD resection started above the UES and was quite difficult because of elongated mucosa, caused by traction of the giant lesion, and due to a lack of working space at the UES level. We succeeded in a complete en bloc resection of the lesion. The patient recovered well, with mild odynophagia during one week, but without obstructive respiratory symptoms. Pathologic evaluation demonstrated a lipoma-like low grade liposarcoma according to a positive MDM2 FISH analysis. Strict follow up is scheduled to detect potential local recurrence.
Conclusion: We describe an ESD resection of a giant pendulated lipomatous lesion at the UES level. This procedure is technically challenging because of the location but could be done with a minimal morbidity for the patient.

- G32 -

ENDOSCOPIC MUCOSAL RESECTION OF RIGHT COLON LATERAL SPREADING TUMOR AND MANAGEMENT OF BLEEDING COMPLICATION. J. Aoun (1), M. Abdessalami (1), M. Figueiredo Ferreira (1), M. Van Gossum (1), P. Eisendrath (1) / [1] CHU Saint-Pierre, Brussels, Belgium, Hepato-gastroenterology.

Video Abstract: We hereby present the case of a 66-year-old male patient, who underwent screening colonoscopy few months ago and was found to have a right-sided, lateral spreading tumour (LST) estimated to 30 mm in diameter. The patient was referred to our institution for endoscopic resection. After careful examination using white light, NBI and near focus, the lesion was described as a granular nodular mixed type LST, Paris IIa+Is, adenoma looking NICE type II, JNET type IIA, and CONECCT type IIA. Submucosal injection of saline and methylene blue induced appropriate lifting sign and revealed a pseudo-pedunculated wide base aspect of the LST. Decision was made to go for en-bloc endoscopic mucosal resection (EMR) using a 25 mm diathermic snare. This allowed resection of the majority of the lesion, leaving behind a small un-resected part at oral edge. Immediate spurting arterial bleeding was observed at the center of polypectomy site. Post EMR intraprocedural bleeding can be managed either by thermal therapy (snare tip soft coagulation/ coagulation forceps) or by mechanical therapy (haemostatic clips). Considering the right sided location and the importance of preserving the small residual polypoid fragment for subsequent resection, we opted for placement of endoclips in order to control the bleed. This was followed by complete resection of the lesion, and soft coagulation of the polypectomy site edges as recommended. In conclusion, this case report illustrates that management of endoscopic resection complications, in particular intraprocedural bleeding, should not impede procedure continuation aiming for a complete resection.

- G33 -

USE OF DOUBLE CLIP RUBBER BAND TRACTION IN A RIGHT COLONIC DISSECTION. J. Zeevaert (1) / [1] CHR Verviers, Verviers, Belgium, Gastroenterology.

Video Abstract: Colonic dissection can be very complicated and risky. Several new techniques and materials are making resection easier and more complex resections can now be performed with greater results. We present the resection of a homogeneous granular LST in the right colon using use of double clip rubber band traction. WeTransfer link for the video: https://we.tl/t-JwIIIb18T4

- G34 -

SALVAGE ENDOSCOPIC FULL THICKNESS RESECTION OF RESIDUAL NEOPLASIA AFTER CHEMORADIATION FOR LOCALLY ADVANCED RECTAL ADENOCARCINOMA. C. Snauwaert (1), J. Van Huysse (2) / [1] AZ Sint-Jan Brugge, Brugge, Belgium, Hepatology and Gastroenterology, [2] AZ Sint-Jan Brugge, Brugge, Belgium, Pathology.

Video Abstract: There is an emerging role for “organ preserving strategies”, i.e. non-surgical management after chemoradiotherapy (CRT) for locally advanced rectal cancer. Performing endoscopic resection for residual lesions after CRT can be challenging due to extensive fibrosis/scarring in the muscularis mucosae and submucosal layers. Endoscopic full thickness resection (EF TR) may offer an effective therapeutic tool for resection of residual lesions after CRT with the potential to avoid (major) surgery. In this video case report, we demonstrate that salvage EFTR after CRT for locally advanced rectal cancer is technically feasible and safe.

- G35 -

SURGERY-SPARING EMR RESCUES FAILED, COMPLICATED ESD FOR A BENIGN RIGHT COLON POLYP INITIALLY SUSPECTED OF SUBMUCOSAL INVASION. P. Poortmans (1), T. Botelberge (2), L. Debels (3), S. Smeets (3), L. Desomer (4), D. Tate (3) / [1] UZ Brussel, Belgium, Gastro-enterology and Hepatology, [2] ZNA Jan Palfijn, Merksem, Belgium, Gastroenterology and Hepatology, [3] Universitair ziekenhuis Gent, Belgium, Gastroenterology and Hepatology, [4] AZ Delta, Roeselare, Belgium, Gastroenterology and Hepatology.

Video Abstract: A large subpedunculated polyp was found in the proximal ascending colon of a 74-year-old male patient. Because of the deformation of the fold by the bulky polyp it contained a risk for covert submucosal invasive cancer, and en-bloc resection was preferred. An endoscopic submucosal dissection was attempted but the circumferential incision was complicated by a perforation Sydney DMI type IV at the oral side of the polyp. The plane was corrected by the senior endoscopist, and dissection was started. Due to the difficult location and suboptimal visualization with extended need of dissection in retroflexion, the resection technique was switched to circumferential submucosal incision and subsequent snare resection (EMR). A 30mm hexagonal snare was used for resection. An arterial bleed was present after the first section of the polyp was resected. A Coagrasper Haemostatic Forceps was used for bleeding control. Subsequently, the second piece of the polyp was resected with the same snare. Again, an important bleed was seen and successfully treated with the Coagrasper. The perforation made during the circumferential incision was closed using 5 clips, after resection of the polyp was completed. The resection defect and margins were coagulated and clipped to reduce the risk of recurrence and late bleeding. The postprocedural period was uneventful. The pathology report showed a traditional serrated adenoma with focal high-grade dysplasia. By not aborting the procedure but instead switching to EMR, the endoscopic resection was salvaged with the patient able to avoid surgery for a non-cancerous polyp.

- G36 -

ENTEROSCOPIC RESECTION OF A PEDUNCULATED POLYP LOCATED IN THE PROXIMAL ILEUM. T. Moreels (1), L. Monino (2) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Hépato-Gastroentérologie, [2] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Hépato-Gastroentérologie.

Video Abstract: We present the case of small bowel bleeding due to an ileal hamartomatous pedunculated polyp, treated with endoscopic polypectomy using single-balloon enteroscopy (SBE). An 80 years old man presented with a history of long-lasting obscure bleeding requiring monthly blood transfusions. He was taking dabigatran because of atrial fibrillation. Gastroscopy and colonoscopy were normal. Wireless video capsule endoscopy was performed and showed an actively bleeding polyp localized in the proximal ileum. An antegrade SBE was planned in order to reach the polyp and to perform polypectomy (Video). Deep antegrade SBE under fluoroscopic guidance allowed to reach the 20 mm ulcerated pedunculated polyp. First, a submucosal tattoo was performed to surgically localize the resection site in case of perforation or incomplete resection. Second, a prophylactic clip was placed on the polyp stalk inducing cyanosis of the polyp’s head. Third, hot snare polypectomy was performed using a medium-size snare with endocut allowing complete resection above the clip without signs of bleeding. The polyp was captured with the snare for histological examination. The total duration of the procedure was 55 minutes. No adverse events were reported. Pathological analysis revelated a hamartomatous polyp with complete resection. At two months, there was no recurrence of anaemia despite the continuous use of dabigatran. This case illustrates the secure resection of an ileal polyp using antegrade single-balloon enteroscopy in a short time and without adverse events.

- G37 -

“APPLE CORE” ESD FOR THE TREATMENT OF A SYMPTOMATIC BRONCHOESOPHAGEAL FISTULA. D. Carpentier (1), S. Ouazzani (1), J. Devière (1), A. Lemmers (1) / [1] HUB Hôpital Erasme Brussels, Brussels, Belgium, Gastroenterology, Hepatopancreatology and Digestive Oncology.

Video Abstract: We report a case of a 20-year-old man with a symptomatic bronchoesophageal fistula. This patient had an history of a type C oesophageal atresia surgically treated during his childhood. He further developed an anastomotic stricture of the ascended intestinal loop which was treated by repeated endoscopic balloon dilations. He progressively presented chronic cough complicated with upper airway chronic secretions and recurrent pneumonitis. A barium swallow

showed an abnormal flow of contrast to the left main bronchi regarding an irregular aspect of the mid oesophageal mucosa. A fistula was endoscopically confirmed with an upper GI endoscopy. An endoscopic procedure was performed with a combination of an "apple core" endoscopic submucosal dissection, APC coagulation and closing with an Endoloop and TTS clips. Radiological follow-up (barium swallow) at 6 weeks showed no residual contrast leakage. The patient was clinically followed after 8 weeks and described less coughing, less respiratory secretions and no recurrence of pneumonitis.

- G38 -

MANAGEMENT OF POST-SPHINCTEROTOMY GI BLEEDING. H. Cherkaoui (1), S. Basbous (2), E. Toussaint (2), D. Blero (2) / [1] CHU de Charleroi, Hôpital Marie-Curie, Charleroi, Belgium, Gastroenterology, [2] CHU de Charleroi, Hôpital Marie Curie, Charleroi, Belgium, Gastroenterology.

Video Abstract: We report the case of an eighty-six-year-old female patient with atrial fibrillation on apixaban, admitted for management of acute pancreatitis of biliary origin. A magnetic resonance confirms the presence of lithiasis in the common bile duct. A retrograde cholangiopancreatography performed after forty-eight hours of the discontinuation of apixaban showed a papilla located between two diverticula on the second duodenum. Cholangiography showed choledochal lithiasis. Sphincterotomy after a precut allowed the stones to be removed. The patient presented hematemesis twenty-four hours after sphincterotomy with a 2-point drop in haemoglobin. The patient was retaken for retrograde cholangiography with the presence of post-sphincterotomy bleeding. After removing the clots with a loop, adrenaline was injected at the sphincterotomy site with a dilution of 1/20,000. A vascular point is identified on the edge of the sphincterotomy, and coagulation of it by the sphincterotome. The procedure ended with placing a 60*10 mm covered, fully covered SeMS stent providing tamponade and drainage. The evolution was favourable with the resumption of anticoagulant without haemorrhage recurrence. The fully covered metallic stent will be removed fifteen days later. In conclusion, pre-cutting and anticoagulant use were the risk factors for post-sphincterotomy haemorrhage found in this patient. Injection of adrenaline serum, coagulation by the sphincterotome, and placement of a tamponade metallic was used to manage the bleeding.

- G39 -

CASE OF ENDOSCOPIC MANAGEMENT OF PER-ERCP PERFORATION. M. Philippart (1), T. De Grez (1), D. Blero (1) / [1] CHR, Namur, Belgium, Service de Gastro-Entérologie.

Video Abstract: Complications from endoscopic retrograde cholangiopancreatography (ERCP) include cholangitis, pancreatitis, bleeding, and perforation. Here we present the case of a 54-year-old woman, who underwent ERCP complicated with perforation. Mrs M. is known for an evoluting pancreatic adenocarcinoma with a malignant gastric outlet obstruction treated with a duodenal stenting in 2021. She was admitted to our hospital in October 2022 for a cholestatic pruritus secondary to a malignant obstruction of the common bile duct. ERCP was indicated to perform a biliary stenting. Major papilla was visible below the distal end of the duodenal stent. ERCP showed one biliary stricture, in regard of the duodenal stent. A sphincterotomy was performed. A new injection of contrast after the sphincterotomy showed a contrast leak in the retroperitoneal space, indicating that the sphincterotomy was complicated by a perforation, classified as Stapfer type II. In our patient, we managed to cover the perforation with an immediate et continuous suction until a fully covered self-expandable metal stent (FCSEMS) was inserted. This allowed endoscopic treatment of biliary stenosis as well as post-ERCP perforation. Our patient also received intravenous antibiotics. Mrs. M. remain asymptomatic in the close follow up and was discharged from hospital the day after ERCP without any other adverse event. Finally our patient experienced a periampullary Stapfer II perforation related to ERCP. Using the surgical Clavien-Dindo classification adapted for endoscopy by Nass et al., the AGREE classification, this adverse event is classified as grade II.

- G40 -

EDGE PROCEDURE GONE WRONG: SWITCH TO NOTES. L. Monino (1), T. Moreels (1) / [1] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Gastroenterology.

Video Abstract:
This videocase shows an endoscopic ultrasound-directed transgastric ERCP (EDGE) with misdeployment of the lumen-apposing metal stent (LAMS) in between the two gastric segments. Using a natural orifice therapeutic endoscopy (NOTES), the LAMS was positioned correctly and the EDGE procedure was completed. A 66-year old male patient with a history of Roux-en-Y gastric bypass (RYGB) underwent cholecystectomy with choledochotomy for bile duct stones. However, he developed a postoperative biliary hilar stricture and was referred for cholangioscopy. Due to the RYGB, the 2-step EDGE procedure was chosen to allow conventional access to the papilla. In the 1st step, the excluded

stomach was visualised from within the gastric pouch and punctured with a 19 G Needle. The lumen of the excluded stomach was filled with liquid. Next, a 0.035 inch Jagwire was introduced into the excluded stomach and a 20*10 mm HotAxios stent was deployed over the guidewire. After LAMS deployment, the distal flange immediately migrated out of the excluded stomach into the peritoneal cavity. The procedure was then switched to a NOTES using a double-channel gastroscope. The LAMS was removed while securing the guidewire into the excluded stomach. Under endoscopic and fluoroscopic control a new LAMS was correctly deployed using the initial gastrogastrostomy fistula. Intraperitoneal CO2 was removed using a percutaneous abdominal needle. Prophylactic antibiotic treatment was given and the patient was able to return home the next day. One week later, the EDGE-ERCP procedure with cholangioscopy was performed through the LAMS.

- G41 -

ENDOSCOPICALLY COMPLETE RESECTION OF AN ESOPHAGEAL SQUAMOUS CARCINOMA INVADING THE MUSCULARIS PROPRIA USING ENDOSCOPIC INTERMUSCULAR DISSECTION. S. Smeets (1), P. Poortmans (1), L. Debels (1), L. Desomer (1), D. Tate (1) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology.

Video Abstract: We present a case of a patient with a squamous cell carcinoma in the distal oesophagus. Due to comorbidities the patient was deemed unfit for surgery. Staging with PET-CT and EUS showed T1N0M0 disease. The patient was discussed during a multidisciplinary discussion, where was decided to proceed with ESD. The endoscopic appearance was that of a large Paris IIa+c lesion in the distal oesophagus with a central depressed ulcer with likely involvement of the muscularis propria. After marking the lesion, a pocket was constructed underneath the central depression, this revealed muscular tethering making intermuscular dissection between the circular and longitudinal muscle layers necessary. After the procedure the patient stayed nil by mouth for 24 hours and was fed nasogastrically for 4 days. After 4 days the patient was started on a liquid diet for 24 hours after which soft foods for 2 weeks. Histopathology showed an invasive carcinoma with lymphovascular invasion, depth of invasion from the muscularis mucosa was 2.2 mm. R1 resection (deep margin positive). The patient will receive additional radio-chemotherapy. The goal of this treatment was debulking, improving symptoms and symptom free interval.

- G42 -

PEDUNCULATED POLYPS RESECTION. J. Zeevaert (1) / [1] CHR Verviers, Verviers, Belgium, Gastroenterology.

Video Abstract: The resection of pedunculated polyps can be complicated and cause bleeding. We present two cases of resection associated with preventive techniques before resection. WeTransfer link for the video : https://we.tl/t-ZUCTPn84yo

- G43 -

ENDOSCOPIC MUSCULAR DISSECTION OF AN OESOPHAGEAL T2 ADENOCARCINOMA IN AN INOPERABLE PATIENT. L. Debels (1), S. Smeets (1), P. Poortmans (1), L. Desomer (2), C. Jorissen (1), T. Lamiroy (1), D. Tate (1) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Department of Gastroenterology and Hepatology, [2] AZ Delta, Roeselare, Belgium, Department of Gastroenterology and Hepatology.

Video Abstract: A 84-year-old male patient was referred for treatment of a suspected T2 adenocarcinoma in a Barrett's oesophagus without nodal or metastatic disease. He was declared inoperable due to medical co-morbidities. After multidisciplinary discussion and after informing the patient about the possible complications and risk of incomplete resection, he agreed to local therapy. An endoscopic submucosal dissection with tunnelling was chosen to start the procedure. This approach allows to first investigate the invasive component and abort the procedure if necessary, without sequelae to the patient. During tunnelling it was clear that both the circular and the longitudinal muscular layers were invaded by tumour and would have to be resected to ensure complete removal. A decision was made to continue given the lack of other therapeutic options for the patient. This resulted in complete perforation with exposure of the adventitia. Once the invasive component was resected, the challenge was to re-establish the submucosal plane. Careful dissection on both sides of the tumoral component made this possible and allowed complete resection of 90% of the oesophageal circumference. After complete resection, a fully covered metal stent was left in situ to cover the perforation. The patient was given intravenous antibiotics and kept nil by mouth for 7 days (TPN). No complications occurred during his hospital stay and he could be discharged after a week. The pathology result showed a poorly differentiated adenocarcinoma with deep margin positive for tumour. Follow-up with consideration of stent removal is planned in 10 weeks.

- G44 -

DOUBLE CLIP RUBBER BAND COUNTER TRACTION FOR COLONIC ESD. A. Lemmers (1), M. Figueiredo Ferreira (1), L. Verset (2), J. Devière (1) / [1] Erasme Hospital, Brussels, Belgium, Gastroenterology, Hepatopancreatology and Digestive Oncology, [2] Institut Jules Bordet, Brussels, Belgium, Pathology.

Video Abstract: A 74-year-old male underwent a colonoscopy revealing a flat 25mm polyp in the transverse colon with features suspicious of superficial cancer. Pictures were obtained and a tatoo was placed. The patient was referred for en-bloc endoscopic resection using ESD. Using a paediatric colonoscope, the lesion was assessed being Paris O-IIb JNET 2B. We proceeded with en-bloc resection by ESD using the double clip- rubber band counter traction technique. The video illustrates the technique and its advantages. Resection was completed en-bloc in clear margins without any complications.

- G45 -

USE OF A TRACTION DEVICE DURING ESD. M. Noreillie (1), S. Jabak (1), H. Ayubi (1), O. Olabintan (1), C. Radia (1), S. Thrumurthy (1), S. Gulati (1), B. Hayee (1), A. Emmanuel (1), A. Haji (1) / [1] King's College Hospital, London, United Kingdom, Endoscopy.

Video Abstract: ESD is an efficient treatment method to achieve en bloc and R0 resection in early-stage gastrointestinal cancers. However, ESD remains challenging and time-consuming with higher risks of adverse events, including bleeding and perforation, as compared to EMR. The fundamental difficulty lies in the accessibility of the submucosal layer during dissection. With a traction device, continuous tissue tension with adequate visualization of the dissection plan can be achieved. In this video we demonstrate the traction method in colonic ESD with the use of a ProdGi traction wire. This method can provide a platform for increased safety profile and decreased procedure time in colorectal ESD.

- G46 -

BALLOON TAMPONADE FOR TREATMENT OF POST-SPHINCTEROTOMY BLEEDING. S. Ouazzani (1), A. Lemmers (2) / [1] Erasme Hospital, Brussels, Belgium, Gastroenterology, [2] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology.

Video Abstract: Post-sphincterotomy bleeding 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 post-sphincterotomy bleeding. The patient had cholestasis with biliary duct dilation in a context of metastatic pulmonary carcinoma, with probable sludge in common bile duct. An ERCP with biliary cannulation was indicated. After the sphincterotomy a venous bleeding occurred. 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.

- G47 -

GASTRIC BAROTRAUMA DURING ESD RESECTION. M. Noreillie (1), R. Bisschops (1), D. De Wulf (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology.

Video Abstract:
Background: Endoscopic Submucosal Dissection (ESD) of oesophageal squamous cell carcinoma (SCC) lesions is a common practice. Often these lesions are multifocal and need subsequent resections. - Case We describe a case of a 60-year-old female patient with previous circumferential ESD resection of a proximal oesophageal SCC, complicated with stenosis 3 years ago and now needing resection of a more distally located new SCC.
Methods: A 15mm balloon dilation of the proximal stenosis was first performed to enable passage of the Olympus GIF-HQ190 endoscope with single-use straight distal attachment cap for ESD (Olympus). The ESD resection was performed with a colonic dual knife and CO2 insufflation with a StratusTM CO2 insufflator at its lowest level. The ESD resection was quick (30 minutes) and uneventful. During recovery time the patient mentioned severe abdominal pain and a pneumoperitoneum was discovered on X-Ray. Repeat endoscopy showed a gastric perforation at the lesser curvature, most likely caused by over-insufflation because of airtrapping due to the gastroscope blocking the narrowed lumen at

the level of the esophageal stenosis. The perforation could best be closed with an OTSC clip but this clip could not pass through the stenosis, so we had to close with conventional resolution clips (Boston Scientific), followed by needle evacuation of the pneumoperitoneum. The patient recovered well without any further complication.
Conclusion: A standard oesophageal SCC ESD resection at a level below an esophageal stenosis was complicated with a pneumoperitoneum secondary to gastric perforation, most likely caused by over-insufflation.

- I01 -

EFFECTIVENESS OF USTEKINUMAB AS THERAPY FOR CHRONIC ANTIBIOTIC REFRACTORY POUCHITIS.
A. Outtier (1), E. Louis (2), O. Dewit (3), G. Schops (1), J. Sabino (1), B. Verstockt (1), S. Vermeire (1), M. Ferrante (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [2] CHU Sart Tilman, Liège, Belgium, Gastroenterology, [3] UCL Saint Luc, Brussels, Belgium, Gastroenterology.

Introduction: Up to 10% of patients with ulcerative colitis who undergo a proctocolectomy with ileal pouch-anal anastomosis, will develop chronic antibiotic refractory pouchitis (CARP).
Aim: As there is a large unmet need in the management of these patients, we evaluated the efficacy and safety of induction and maintenance therapy with ustekinumab (UST).
Methods: We performed a prospective, Belgian, multicentre, open-label study of patients with CARP (mPDAI ≥5 with an endoscopic subscore ≥2) . Patients received a weight-range-based infusion of UST at baseline (~6mg/kg) and subcutaneous injections of 90mg UST every 8 weeks thereafter until week 48. Patients underwent a pouchoscopy at baseline, week 16 and week 48, with assessment of the modified pouchitis disease activity index (mPDAI). The primary endpoint was the proportion of patients achieving steroid-free remission (mPDAI <5 and reduction by ≥2 points from baseline) at week 16. For this abstract we focus on the secondary endpoints at week 48 including the proportion of patients achieving steroid-free remission and response (reduction of mPDAI by ≥2 points from baseline) using a non-responder imputation. For patients still continuing UST at week 48, we evaluated the change in symptomatic and endoscopic mPDAI subscore, C-reactive protein (CRP) and faecal calprotectin levels compared to baseline. Descriptive statistics and paired nonparametric tests (Wilcoxon signed-rank) of changes from baseline were performed.
Results: We enrolled 22 patients (59% male, median age 42.2 years, median time after surgery 8.2 years). Twelve (54.5%) patients had previously been treated with biologics for CARP. At week 16, steroid-free remission was achieved in 27.3% of patients. At week 48, steroid-free remission was achieved in 36.4% and response in 54.5% of patients. In the 14 patients continuing UST at week 48, a significant decrease in total mPDAI (4 (1.8-7.3) vs. 8 (8-10), p<0.001), clinical subscore (1 (0-2.3) vs. 3 (2-4), p=0.001), and endoscopic subscore (3 (1.8-4.3) vs. 6 (4.8-6), p=0.001) was observed compared to baseline. Faecal calprotectin (129 (80-344) vs. 229 (139-541) mg/kg, p=0.17) and CRP (2.5 (1.3-4.4) vs. 3.8 (1.6-9.3) mg/L, p=0.09) levels did however not decrease significantly. Three serious adverse events (hospitalization for subobstruction, worsening pouchitis and choledocholithiasis) were recorded, but were not considered related to UST.
Conclusions: In this open-label pilot study in patients with CARP, maintenance therapy with UST showed a clinical and endoscopic effect in half of the patients but was not associated with changes in inflammatory biomarkers. These promising results warrant confirmation in a placebo-controlled study with UST for the treatment of CARP.

- I02 -

USTEKINUMAB IN ULCERATIVE COLITIS: A REAL-LIFE EFFECTIVENESS STUDY ACROSS MULTIPLE BELGIAN CENTERS (SULTAN).
T. Holvoet (1), M. Truyens (2), C. Reenaers (3), F. Baert (4), S. Vandenbranden (5), A. Cremer (6), L. Pouillon (7), P. Dewint (8), W. Van Moerkercke (9), J. Rahier (10), L. Vandermeulen (11), J. Van Dongen (12), H. Peeters (13), G. Lambrecht (14), A. Vijverman (15), T. Lobaton (2) / [1] Vitaz, Sint-Niklaas, Belgium, Gastroenterology, [2] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology, [3] CHU of Liège, Belgium, Gastroenterology, [4] AZ Delta, Roeselare, Belgium, Gastroenterology, [5] OLV Aalst, Aalst, Belgium, Gastroenterology, [6] Hopital Erasme, ULB, Belgium, Gastroenterology, [7] Imelda Hospital, Bonheiden, Belgium, Gastroenterology, [8] AZ Maria Middelares, Ghent, Belgium, Gastroenterology, [9] AZ Groeninge, Kortrijk, Belgium, Gastroenterology, [10] CHU UCL Namur, Yvoir, Belgium, Gastroenterology, [11] UZ Brussel, Belgium, Gastroenterology, [12] AZ Sint Maarten, Mechelen, Belgium, Gastroenterology, [13] AZ Sint-Lucas, Ghent, Belgium, Gastroenterology, [14] AZ Damiaan, Oostende, Belgium, Gastroenterology, [15] CHR Citadelle, Liège, Belgium, Gastroenterology.

Introduction: Ulcerative colitis (UC) is a chronic inflammatory disease affecting the colon (1). Ustekinumab (UST), a monoclonal antibody against the p40 subunit of interleukin (IL) 12 and 23 has shown in the UNIFI trials to be effective and safe in patients with moderate-to-severe UC (2). Real-life data are still limited (3).
Aim: To assess the real-world effectiveness and safety of UST in patients with UC across Belgian hospitals.
Methods: In this multicentric, retrospective observational study, patients with UC who received UST from September 2020 onwards were included. Clinical, endoscopical and biochemical response was assessed at baseline, week 8, 16 and 52. The primary endpoint was steroid-free remission defined as partial Mayo score of ≤ 2 with no subscore > 1 at week 16. Secondary endpoints included endoscopic remission (endoscopic Mayo = 0), endoscopic, clinical and biochemical response (defined respectively as an endoscopic Mayo score ≤ 1, a decrease from baseline in partial Mayo score (stool frequency and rectal bleeding) by ≥ 1 and ≥ 30% and a decline of 50% or more in CRP and/or faecal calprotectin).
Results: 107 patients with moderate-severe UC (86% patients with ≥ S2 severity) were included across 16 participating centers. Median disease duration was 10 years (1-73y) and 69 (64%) of patients had previously failed 2 or more

biologicals. At week 16, 35 patients reached the primary endpoint of steroid-free clinical remission (33%), while 67 had a clinical response (62.6%) (Fig 1). Endoscopic response was noted in 44 patients (41%) with remission reached in 19 patients (18%). Biochemical response was seen in 41 patients (38%). There was a statistically significant decline in partial mayo score (median at baseline 6.0 range (1-9); W16 2.0 (0-9, p<.001), CRP (3.85 mg/L (0.4-181) vs 3.15 (0.88-10.3); p<.001) and calprotectin (1040 (13-6000) vs 300 (3.8-2980); p<.001) (Fig 2 and 3). No predictors for steroid-free remission could be identified. At the end of follow-up at week 52, 75 patients were still treated with UST (70%). Reasons for discontinuation were primary non-response (N=18 (17%), loss of response (N=8 (7.5%) and adverse events (N=2 (1.9%)). No predictor for UST failure could be identified. Eight patients needed to be referred for colectomy (7.5%). In 7 patients dose optimization via IV reinduction occurred. No difference in occurrence of extra-intestinal manifestations was noted during treatment, severe infections occurred in 1 patient (0.9%). No other new safety signals were observed.
Conclusions: In this multi-centric, real-life cohort with highly refractory UC patients, UST was associated with a clinical response rate of 63% at 16 weeks while steroid-free remission was achieved in 33% of patients. Endoscopic response was achieved in 41%, with endoscopic remission in 18% of patients. No important new safety signals were observed.

- I03 -

USTEKINUMAB IS THE PREFERRED BIOLOGICAL AGENT IN IBD PATIENTS WITH HIDRADENITIS SUPPURATIVA FAILING ANTI-TNF THERAPY : RESULTS FROM A REAL-LIFE MULTICENTER COHORT.
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Introduction: Hidradenitis suppurativa (HS) is a chronic, recurrent inflammatory disease affecting skin that bears apocrine glands and is characterised by painful, deep-seated, inflamed lesions. Treatment includes antibiotics, steroids, surgery, and adalimumab as the only approved biological agent. An association between inflammatory bowel disease (IBD) and HS has been reported, but very limited evidence exists on the efficacy of non-anti-TNF biological agents for the treatment of HS in IBD patients.
Aim: To report the efficacy of non-anti-TNF agents in the treatment of hidradenitis suppurativa in patients with inflammatory bowel diseases.
Methods: This multicenter case series was performed as part of the Collaborative Network of Exceptionally Rare case reports (CONFER) project by ECCO. Cases of patients with HS and IBD treated with non-anti-TNF biological agents were retrospectively collected through a standardised collection form. Efficacy measures were reported by the local gastroenterologist/dermatologist using physician global assessment (PGA).
Results: Fifty-five patients (65.5% women, median [IQR] age 40.0 [33.1-47.6] years, 50.9% active smokers) were identified, all with HS diagnosis confirmed by a dermatologist. We observed a strong CD predominance (90.9%) in the current cohort. HS affected mainly the inguinal (82.0%) and axillary (76.0%) regions, followed by the anogenital region (46.0%). In 42 patients, HS was diagnosed a median of 10.0 [4.3-16.4] years after the IBD diagnosis, whereas in 13 HS preceded the IBD diagnosis by 4.1 [2.2-5.4] years. Prior to initiating a non-anti-TNF biological agent, all patients had been exposed to at least 1 anti-TNF agent, including (high dose) adalimumab in 83.2% of the cases. In 20% of patients, HS developed while being treated with an anti-TNF agent. After anti-TNF failure (for either IBD and/or HS), physicians opted for ustekinumab (83.6%), vedolizumab (14.5%), or risankizumab (1.8%) as the preferred first non-anti-TNF agent. During ustekinumab treatment (n=46, median time on therapy 2.1 [0.8-3.3] years)), 76.1% showed a clinically relevant HS improvement (including 50.0% complete remission), whereas 23.9% did not experience any benefit. With vedolizumab (n=8), 37.5% experienced some benefit (including 25.0% with complete remission), while 62.5% did not

report any improvement. The single patient on risankizumab had complete remission. Finally, 6 out of 8 vedolizumab-treated patients were ultimately treated with ustekinumab, reporting a clinical benefit in 5 out of 6.
Conclusions: Ustekinumab is the preferred biological agent after anti-TNF failure in IBD patients with concomitant HS. Although placebo-controlled trials are lacking and ustekinumab is not approved for the treatment of HS, the current multi-centre case series demonstrates a substantial benefit in 78.4% of patients.

- I04 -

DEFINING A CORE SET OF MEASUREMENTS FOR QUALITY OF CARE FOR PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN BELGIUM. L. Fierens (1), P. Bossuyt (2), F. Baert (3), D. Baert (4), M. Lavaerts (5), C. Weltens (5), M. Ferrante (6) / [1] KUL - University of Leuven, Leuven, Belgium, Translational Research Center for Gastrointestinal Disorders (TARGID), Department of Chronic Diseases, Metabolism, and Ageing, [2] Imelda Hospital, Bonheiden, Belgium, Imelda GI Clinical Research Centre, [3] AZ Delta, Roeselare, Belgium, Department of Gastroenterology, [4] AZ Maria Middelares, Ghent, Belgium, Department of Gastroenterology, [5] KUL - University of Leuven, Leuven, Belgium, Flemish Hospital Network, [6] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Uniform and standardized quality indicator (QI) measurement allows to assess quality of care (QoC) and set up quality improvement initiatives. To date there is no uniform measurement of QoC in IBD centres in Belgium.
Aim: We therefore aimed to adapt existing standards of QoC to practical local needs, and to define a core set of quality measurements (QM) through a multi-stakeholder consensus.
Methods: A Core Team (4 IBD expert clinicians, 3 researchers) prepared and coordinated the Delphi process. Through a literature review, 221 existing QIs for IBD were identified. Second, an importance rating scale exercise was performed, leading to 58 QIs that were reformulated into practical QMs. Next, a variety of experts from different centres in Flanders were invited to rate the importance of these 58 QMs on a 10-point Likert scale. In between two consecutive online voting rounds, expert and patient (n=93) perspectives were provided. Furthermore, participants could also suggest items that were missing in the pre-selected list. A consensus threshold of ≥80% of the participants scoring the item 7, 8, 9 or 10 in voting round 2 was applied as the cut-off criterion for an item to be directly included in the final set of QMs. Newly suggested items and items that did not reach the cut-off criterion were discussed and reconsidered for inclusion in the final set during a closing consensus meeting. In order to come to a workable selection of items, participants to the consensus meeting were requested to estimate the potential for improvement of each of the selected QMs.
Results: In total 40 stakeholders of which 29 IBD clinicians, 7 IBD nurses, 2 paediatricians, 1 abdominal surgeon and 1 chief medical officer from 24 different Flemish centres participated in both Delphi voting rounds. Of this group, 21 IBD clinicians, 3 IBD nurses and 2 paediatricians also participated in the virtual consensus meeting. In total, 50 items reached the cut-off criterion for direct inclusion in the final QM set, the other 8 items and also 3 new items were discussed and re-voted during the consensus meeting of which 8 additionally reached the cut-off criterion to include in the final set. Based on the estimated improvement potential, 19 of these 58 QMs were prioritized and agreed to measure in clinical practice. This subset of 19 QMs with potential for improvement included measurements of medication, use of hospital services, post-intervention events, infections, routine follow-up, disease activity and patient-reported outcomes.
Conclusions: We defined a core set of 58 QMs for IBD based on multi-stakeholder consensus. In the next phase of this project, a more condensed subset of 19 QMs with potential for improvement will be measured in IBD centres across Belgium, allowing QoC assessment, benchmarking and quality improvement initiatives.

- I05 -

THE HEALTH OUTCOMES OBSERVATORY (H2O) CORE DATA SET FOR PATIENTS WITH INFLAMMATORY BOWEL DISEASE: PRACTICAL RECOMMENDATIONS FOR THE COLLECTION OF INCLUDED PATIENT-REPORTED OUTCOMES. L. Fierens (1), C. van der Woude (2), A. Huberts (3), F. Casellas (4), N. Borruel (4), B. Siegmund (5), E. Sonnenberg (5), G. Novacek (6), N. Gerold (6), T. Stamm (7), C. Hedin (8), M. Julsgaard (9), G. Fiorino (10), S. Radice (10), M. Zini (11), E. Gross (12), C. Sander (13), I. Arijs (14), V. Vakouftsi (15), N. Carney (16), I. Charlafti (17), M. Ferrante (18) / [1] KUL - University of Leuven, Leuven, Belgium, Translational Research Center for Gastrointestinal Disorders (TARGID), Department of Chronic Diseases, Metabolism, and Ageing, [2] Erasmus MC, University Medical Center Rotterdam, The Netherlands, Dept. of Gastroenterology, [3] Erasmus MC, University Medical Center Rotterdam, The Netherlands, Quality and patientcare, [4] Hospital Universitari Vall d'Hebron, , Spain, Crohn-Colitis Unit, [5] Charité Universitätsmedizin Berlin, Germany, Medizinische Klinik für Gastroenterologie, Infektiologie, Rheumatologie, [6] Medical University of Vienna, , Austria, Department of Internal Medicine III, [7] Medical University of Vienna, Austria, Institute for Outcomes Research, Center for Medical Statistics, Informatics and Intelligent Systems, [8] Karolinska Institutet, Karolinska University Hospital, Sweden, Department of Medicine Solna, [9] Aarhus University Hospital, Aarhus, Denmark, Aarhus, Denmark, Department of Hepatology and Gastroenterology, [10] Vita Salute San Raffaele University, Milan, Italy, Department of Gastroenterology, [11] Vita Salute San Raffaele University, Milan, Italy, School of Medicine, [12] Österreichische Morbus Crohn / Colitis ulcerosa Vereinigung (ÖMCCV), Austria, President,

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Introduction: Large scale data integration and comparison require standardised data collection. As part of the Health Outcomes Observatory (H2O) project, a core data set for IBD (including case-mix variables, biomarkers, clinical and patient-reported outcomes) that can uniformly be implemented across IBD centres was defined through an international, multi-stakeholder Delphi process. Fierens L et al, UEG Week 2022.
Aim: The aim in this next step of the project was to identify the most appropriate instruments and minimum frequency to measure the patient-reported outcomes included in this core data set.
Methods: A group of key stakeholders assessed potential instruments that were identified through a literature review. The literature review report included details on the development process, validation studies, extensiveness, required licenses and available translations of the identified instruments. The stakeholders were then asked to indicate in a survey which instrument(s) they considered most important to include in the core data set and at what minimum frequency they would collect these data. The collected insights were discussed at an online consensus meeting in Sept 2022 where a final selection of instruments and minimum frequency was agreed on.
Results: In total, 18 stakeholders from 10 different countries completed the survey (7 IBD specialists, 4 patient advocates, 3 pharma experts, 2 IBD nurses, 1 expert in patient-reported outcome measurements and 1 regulator). Also 18 stakeholders attended the consensus meeting (6 IBD specialists, 5 patient advocates, 3 academic researchers, 3 pharma experts and 1 IBD nurse from 11 different countries). The PRO-2 (both for UC and CD) and the IBD-Control were indicated as the most appropriate instruments to collect the IBD-specific outcomes, and the PROMIS Global Health and PROMIS Self-Efficacy short form to collect the generic patient-reported outcomes. At the consensus meeting it was additionally agreed to use the generic Health Monitor (disease acceptance and control) and to supplement the set with additional single items to measure bowel incontinence, bowel urgency, IBD medication adherence and the extent to which patients feel informed. It was agreed that the IBD-specific outcomes would be collected at every consultation with an IBD practitioner, with a minimum of once every twelve months and a maximum of once every three months. The generic outcomes would be collected with a minimum of once every twelve months, and a maximum of once every three months.
Conclusions: This study recommends an instrument set and minimum frequency to measure the patient-reported outcomes included in the H2O core data set for IBD, agreed on by a group of key stakeholders. This set will initially be implemented in five European university clinics and subsequently in additional IBD clinics, enabling data integration and comparisons on a larger scale.

- I06 -

ASSESSMENT OF THE ONE-YEAR EFFICACY AND SAFETY OF TOFACITINIB IN BIOLOGIC-REFRACTORY PATIENTS WITH ULCERATIVE COLITIS: A REAL-WORLD BELGIAN COHORT STUDY. A. Cremer (1), A. Mansour (1), T. Lobaton (2), S. Vieujean (3), P. Bossuyt (4), J. Rahier (5), F. Baert (6), O. Dewit (7), E. Macken (8), A. Vijverman (9), P. Van Hootegem (10), F. Mana (11), B. Willandt (12), E. Humblet (13), F. D'Heygere (14), A. Verreth (15), A. El Nawar (16), J. Coenegrachts (17), S. Dewit (18), S. De Coninck (19), N. Schoofs (20), S. Delen (21), J. Dutre (22), C. Thienpont (23), S. Vanden Branden (24), D. Staessen (25), C. Croonen (26), D. Franchimont (1) / [1] Erasme Hospital, Brussels, Belgium, Gastroenterology, [2] University Hospital of Ghent, Belgium, Gastroenterology, [3] CHU Sart- Tilman, Liège, Belgium, Gastroenterology, [4] Imelda Hospital, Bonheiden, Belgium, Gastroenterology, [5] Centre Hospitalier Universitaire Mont-Godinne, , Belgium, Gastroenterology, [6] AZ Delta, Roeselare, Belgium, Gastroenterology, [7] Saint-Luc University Hospital, Brussel, Belgium, Gastroenterology, [8] Antwerp University Hospital, Edegem, Belgium, Gastroenterology, [9] Hospital CHR de la Citadelle, Liège, , Belgium, Gastroenterology, [10] AZ Sint-Lucas Brugge, Assebroek/ Brugge, Belgium, Gastroenterology, [11] Clinique Saint-Jean, Brussels, Belgium, Gastroenterology, [12] AZ Sint-Jan Brugge-Oostende, Brugge, Belgium, Gastroenterology, [13] Ziekenhuis Oost Limbug (ZOL), Genk, Belgium, Gastroenterology, [14] AZ Groeninge, Kortrijk, Belgium, Gastroenterology, [15] AZ Voorkempen, Belgium, Gastroenterology, [16] Centre Hospitalier Mouscron, Mouscron, Belgium, Gastroenterology, [17] Jessa Hospital, Hasselt, Belgium, Gastroenterology, [18] Mariaziekenhuis Noord-Limburg, Overpelt, Belgium, Gastroenterology, [19] Sint-Andries Ziekenhuis Tielt, Tielt, Belgium, Gastroenterology, [20] Sint-Trudo ziekenhuis, Sint-Truiden, Sint-Truiden, Belgium, Gastroenterology, [21] ZH Maas en Kempen, Belgium, Gastroenterology, [22] ZNA Jan Palfijn, Merksem, Belgium, Gastroenterology, [23] ZNA Antwerpen, Antwerpen, Belgium, Gastroenterology, [24] Onze-Lieve-Vrouw Ziekenhuis, Aalst, Belgium, Gastroenterology, [25] GZA Sint-Vincentius ziekenhuis, Antwerpen, Belgium, Gastroenterology, [26] AZ TURNHOUT, Turnhout, Belgium, Gastroenterology.

Introduction: Tofacitinib, an oral Janus kinase inhibitor, has been approved in 2018 for the treatment of moderate to severe ulcerative colitis (UC) in Europe. Efficacy and safety data from long-term real-world studies are scarce.

Aim: The aim of the study was to evaluate the real-world long-term efficacy and safety of tofacitinib in a Belgian cohort of patients with refractory UC who were exposed to both anti-TNF and vedolizumab.
Methods: We performed an observational, national, retrospective multicenter study including all patients with active UC who started on tofacitinib between November 2018 and August 2019 in 26 Belgian centers (Ethics Committee approval number P2019/429, date: 10/12/2019; amendment for study extension received on 16/07/2020). Data were prospectively collected and retrospectively analysed according to intention-to-treat. Clinical response (decrease from baseline in partial adapted Mayo score (stool frequency and rectal bleeding) by ≥ 1 and ≥ 30%), clinical remission (Partial Adapted Mayo score ≤ 1), steroid-free clinical remission, endoscopic response (decrease from baseline in Mayo endoscopic subscore of ≥ 1), endoscopic remission (endoscopic Mayo subscore of 0), drug survival, need for colectomy and adverse events (AEs) were assessed at week 8, 16 and 52.
Results: A total of 75 patients were included with a median follow-up of 45 weeks (IQR: 19-51). Patients were predominately men (59%), and median age at baseline was 44 years (IQR: 31-59). Median disease duration was 8 years (IQR: 4-17). Fifty-five percent had left-sided UC and 45% had pancolitis. Overall, 72 (96%), 51 (68%) and 6 (8%) patients were exposed to at least 1, 2 or 3 antiTNFs respectively, and 73 (97%) to vedolizumab. At baseline, 42 (56%) patients were under steroids. Median Partial Adapted Mayo score at baseline was 4 (IQR: 3-5), and median endoscopic Mayo subscore was 2 (IQR: 2-3). Thirty-nine (52%) patients required prolonged induction at 10mg twice daily for 8 additional weeks. Dose optimization was needed in 12 (16%) patients due to disease relapse after induction response, 9 (12%) of which could regain response. After 1 year, 52% and 43% of patients had experienced clinical response and clinical remission respectively, and 39% achieved steroid-free clinical remission. Endoscopic response and remission were observed in 37% and 9% of patients. Faecal calprotectin < 250 µg/g at week 16 (OR: 0.03(95%CI: 0.003-0.4)) was a positive predictor of clinical remission at week 52. Overall, 34 (45%) patients discontinued tofacitinib (22 due to primary non-response, 11 due to secondary loss of response and 1 due to AE) during follow-up with a median exposure duration of 17 weeks (IQR: 11-42). Among these patients, 6 underwent colectomy for disease worsening after a median treatment duration of 15 weeks (IQR: 11-19) and a median follow-up of 20 weeks (IQR: 12-25), while the others switched to another medical therapy. Forty AEs were reported in 25 (33%) patients, with only one (pneumonia) leading to treatment discontinuation. The most common AEs were arthralgia and lower respiratory tract infections followed by herpes zoster, urinary tract and upper respiratory tract infections. Two cases of prostate cancer have been reported. No opportunistic infection, venous thromboembolism, pulmonary embolism or cardiovascular event were reported. A statistically significant increase of 43% in the low-density lipoprotein (LDL) level was observed between baseline and week 52 among patients in clinical remission at week 52, with no significant changes in total cholesterol and high-density lipoprotein (HDL).
Conclusions: Tofacitinib effectively induced long-term clinical and endoscopic response and remission in a refractory cohort of patients with UC in a real-world clinical setting. During this one-year follow-up, tofacitinib was relatively well tolerated with respect to adverse events.

- I07 -

NO INCREASED POSTOPERATIVE RISK OF VENOUS THROMBOEMBOLISM NOR INFECTIOUS COMPLICATIONS AFTER JAK INHIBITOR EXPOSURE IN PATIENTS WITH ULCERATIVE COLITIS UNDERGOING COLECTOMY. I. De Greef (1), G. Bislenghi (2), I. Terrasson (2), J. Sabino (3), M. Ferrante (3), A. D'Hoore (2), S. Vermeire (3), B. Verstockt (3) / [1] KUL - University of Leuven, Leuven, Belgium, Chronic Diseases and Metabolism (CHROMETA), [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Abdominal surgery, [3] KU Leuven - University of Leuven, Leuven, Belgium, Chronic Diseases, Metabolism and Ageing (CHROMETA).

Introduction: Total colectomy for ulcerative colitis (UC) is associated with postoperative morbidity, including venous thromboembolism (VTE), in patients who already have a 2 to 4-fold risk for thromboembolic events.
Aim: In light of recent concerns on increased major adverse events associated with JAK inhibitor exposure, we aimed to evaluate the postoperative VTE risk as well as other complications in UC patients undergoing colectomy after use of JAK inhibitors.
Methods: This retrospective cohort study included all UC patients who underwent (procto)colectomy between 2013 and 2021 in our tertiary IBD center and documented the 180-day postoperative non-infectious and infectious risks. Clinically relevant information included patient demographics, comorbidities, family history of IBD, personal history of VTE, intake of oral anticonception, smoking behaviour, disease characteristics including indication for colectomy, preoperative serum laboratory values, perioperative drug exposure, and use of low-molecular weight heparin (LMWH) prophylaxis.
Results: One-hundred seventy-nine UC patients (43.6% women, median [IQR] age 42.0 [28.5 – 56.2] years) underwent colectomy due to refractory disease (n=154) or suspected dysplasia or cancer (n=25). Forty-nine patients (27.4%) were operated urgently. In the twelve weeks prior to surgery, 55 (30.7%) patients had received anti-TNF agents, 40 (22.3%) anti-adhesion therapy, 16 (8.9%) anti-IL12/23, 2 (1.1%) investigational agents and 36 (20.1%) JAK inhibitors. Preoperatively, 27 patients (15.1%) were administered a moderate to high dose of systemic corticosteroids (at least 20 mg/day of methylprednisolone or equivalent for > 8 weeks). All patients received antithrombotic prophylactic LMWH

postoperatively (median 20 days), except for two patients who developed a gastrointestinal bleeding. During the 180-day postoperative period, a total of 3 patients (1.7%; mean age 51 years, 1 female) developed an intra-abdominal thrombosis, found by coincidence on CT scan. In all 3 patients other risk factors were identified, e.g. inflammatory state, cancer, high dose of corticosteroids. No VTE was seen in the patients who underwent colectomy while on JAK inhibitor. Only two out of 36 JAK inhibitor treated patients (5.6%) developed an infectious complication, while the overall risk of developing an infectious complication was 19.5%.
Conclusions: The overall risk for UC patients to develop VTE after colectomy is low with adequate antithrombotic prophylactic therapy. We did not observe any VTE in patients who were exposed to JAK inhibitors prior to surgery, nor did we see an increased risk on short-term infectious complications in this patient group. All patients who developed VTE despite LMWH had additional risk factors.

- I08 -

INTRODUCING VIDEO CONSULTATIONS AS PART OF AN IBD TIGHT MONITORING CARE PATHWAY: INTERIM RESULTS OF THE INTERACTION PROJECT. E. Hoefkens (1), N. Lembrechts (1), P. Bossuyt (1), L. Pouillon (1) / [1] Imelda Hospital, Bonheiden, Belgium, Gastroenterology.

Introduction: IBD requires tight monitoring of disease activity. E-health and tele-health applications are associated with improved clinical outcomes and have a positive impact on healthcare costs.
Aim: INTERACTION (telemedIciNe as parT of an intEgRAted IBD Care paThway @Imelda bONheiden) is a pilot project exploring the feasibility of implementation of teleconsultation in an existing tight monitoring care pathway, potential (dis)advantages for patients and health-care workers, and the impact on the quality-of-care.
Methods: INTERACTION is an ongoing, single-centre feasibility project prospectively including patients with moderate-to-severe IBD (UC/CD) treated with immunomodulators, subcutaneous biotherapy or oral small molecules since February 2022. Eligibility criteria include (i) stable treatment and remission, based on physician global assessment, patient-reported outcomes (UC: SCCAI<3; CD: PRO-2 ≤11), and faecal calprotectin (<250 µg/g) or endoscopy (UC: MES ≤1; CD: SES-CD ≤5), and (ii) digital access. Participants agreed to embark in an adapted IBD care pathway implementing video consultations with the treating physician alternating with in-person consultations. PRO's were collected before both video consultations and in-person consultations, while biomarkers were only collected at in-person consultations. Patients' expectations were questioned at the start of the care pathway. Outcomes included patients' experiences (assessed with the adapted Telehealth Usability Questionnaire), socio-economic impact, and clinical evolution (IBD-related flares or hospitalisations).
Results: At the moment of interim analysis (Oct 24th, 2022), 37/44 (84%) invited patients wanted to participate. The majority expected that teleconsultations could be equal to in-person consultations (86%) and lead to an increased access to healthcare (92%) and time gain (97%). Seven patients refused participation for various reasons (fear of missing in-person consultation with physician; timing of video consultations conflicting with work hours; lack of video; no anticipated benefit (n=2); no interest in digital world (n=2)). Four patients were screen failures due to lack of remission. Ultimately, 33 patients (19 male/14 female; 28 CD/5 UC) underwent a total of 67 consultations. Treatments at baseline were oral puri-nethol (3%), adalimumab SC (64%), ustekinumab SC (9%), vedolizumab SC (9%) or infliximab SC (15%). All patients were in clinical (median (IQR) PGA 0 (0-0), PRO2 6.5 (2-22) for CD, and SCCAI 4 (1-15) for UC) and biochemical (median (IQR) calprotectin level 46 (13-139) mg/kg) remission at the start of the care pathway. The majority (92%) experienced the video consultations as (strongly) satisfactory. All patients agreed to use telehealth services again in the future. Patients' time savings with video consultation compared to an in-person consultation varied between 0-30' (16%); 30-60' (36%), 60-120' (36%) and more than 120' (12%). Patients avoided a round trip to the hospital between 0-10 km (8%), 10-30 km (56%), 30-80 km (24%) or more than 80 km (12%). Forty percent averted absenteeism. One patient experienced an IBD flare without the need for hospitalisation during the median follow-up of 3 (IQR 3-5.5) months.
Conclusions: Implementing video consultations in the IBD care pathway of the ongoing INTERACTION project seems feasible, well-received and safe in patients with IBD in stable remission. In a second phase, video consultations led by an advanced IBD-nurse warrant further exploration.

- I09 -

PATTERNS OF CORTICOSTEROID EXPOSURE AND EXCESS IN INFLAMMATORY BOWEL DISEASE IN BELGIUM: RESULTS FROM THE DETERMINANTS, INCIDENCE AND CONSEQUENCES OF CORTICOSTEROID EXCESS (DICE) ONLINE MONITORING TOOL. P. Bossuyt (1), F. D'Heygere (2), J. Schrevens (3), J. Morrens (3), E. Louis (4) / [1] Imelda Hospital, Bonheiden, Belgium, Department of Gastroenterology, [2] AZ Groeninge, Kortrijk, Belgium, Department of Gastroenterology, [3] AbbVie Belgium SA, Wavre, Belgium, Medical Affairs, [4] CHU de Liège, Liège, Belgium, Department of Gastroenterology.

Introduction: Corticosteroids (CS) are indicated for inducing response in inflammatory bowel disease (IBD), yet due to side effects their long-term use as maintenance therapy is limited.1 While alternative treatments are available and

guidelines1-4 recommend on steroid-sparing strategies and its use as a quality indicator, CS dependency and CS excess remain common in clinical practice. However, as for many other countries, it is unknown how often use and excess use of CS are present in Belgium.
Aim: This real-world study aimed to quantify CS exposure and CS excess in daily clinical practice of IBD in Belgium.
Methods: Belgium participated in a multi-country, cross-sectional study aimed at quantifying the incidence of CS use in patients with IBD using an online CS monitoring tool. Each center also completed a service-level questionnaire. Patients were included if they were ≥18 years and had a diagnosis of IBD for >1 year. Outcomes assessed were CS exposure within the last 12 months, and CS excess (defined as >1 course of CS or use for ≥3 months within the last 12 months, or an inability to reduce CS below the equivalent of prednisolone 10 mg/day or budesonide 3 mg/day within 3 months of starting CS without IBD recurrence, or relapse within 3 months of stopping CS). Proportions of patients with CS exposure and CS excess were reported. To evaluate the influence of independent variables on occurrence of CS exposure and CS excess, single variable and multivariable logistic regression was used. From these models, OR's along with p-values were evaluated.
Results: Data from 250 Belgian patients with IBD in 3 centres were analysed (Crohn's disease [CD], n=164; ulcerative colitis [UC], n=86). In total, 23% of patients were exposed to CS and 16% had excess use of CS. Rates of CS exposure and excess were numerically higher in patients with UC versus CD (exposure: 28% versus 21%, p=0.23; and excess use: 19% versus 14%, p=0.32, respectively). Patients with moderate to severe disease had significantly higher rates of CS exposure and CS excess use compared to patients with inactive/quiescent to mild disease (CS exposure: 79% vs 16% respectively, OR=20.4, p <0.0001; CS excess: 62% vs 10% respectively, OR=15.6, p<0.0001). For patients with inactive/quiescent disease, 9.3% (14/151) were exposed to CS. While the overall UC group contained numerically higher proportions of CS exposure and excess compared to the overall CD group, moderate to severe CD led to higher rates of CS exposure and excess compared to UC with similar disease activity (CS exposure: 84% vs 70%; CS excess: 68% vs 50%). The probability of CS exposure and excess numerically increased with the number of previous targeted therapies for CD, but not for UC. Multivariable analysis confirmed that disease severity contributed significantly to CS exposure and excess in patients with both CD and UC. Further, multivariable modelling revealed a significant positive association between CS exposure and current use of thiopurines in CD (OR: 7.86, p= 0.021) but not UC.
Conclusions: The present cross-sectional study found that among IBD patients in Belgium, use of corticosteroids remains relatively common: within the last 12 months, 23% were exposed to CS and 16% had excess use. Disease severity (moderate/severe vs mild/quiescent) was associated with an increased risk of CS exposure and excess in patients with CD and UC, yet CS exposure was still present in patients with inactive/quiescent disease. Exposure and excess use of CS was associated with a higher number of prior targeted therapies in CD, but not UC. Finally, multivariable modelling revealed a positive association between current use of thiopurines and CS exposure in CD, but not UC.

- I10 -

BEHAVIOUR IN MICE WITH CHRONIC DSS COLITIS MIMICS FATIGUE IN IBD AND IS ASSOCIATED WITH NEUROINFLAMMATION. M. Truyens (1), H. Lernout (2), C. Vandendriessche (3), A. Bruggeman (4), J. Xie (3), M. De Vos (1), V. Vermeirssen (5), R. Vandenbroucke (3), D. Laukens (1) / [1] Ghent University, Ghent, Belgium, Internal Medicine and Paediatrics, [2] Universiteit Gent, Gent, Belgium, Internal Diseases and Paediatrics, [3] Ghent University, Ghent, Belgium, VIB Centre for Inflammation Research (IRC), [4] University Hospital Ghent (UZ Gent), Gent, Belgium, Neurology, [5] Ghent University, Ghent, Belgium, Biomedical Molecular Biology.

Introduction: Inflammatory bowel diseases (IBD) are often associated with psychological comorbidities such as fatigue. Up to 47% of patients report fatigue despite disease remission.
Aim: The aim of the current study was to assess neurobehavioural changes in a mouse model of extinguished chronic colitis and to explore associated changes along the gut-brain axis.
Methods: Repeated administration of 2% dextran sulphate sodium (DSS) was used to induce chronic colitis in C57BL/6 mice, followed by a recovery period of 3 weeks to mimic quiescent IBD. Behavioural testing was performed at baseline and after the recovery period and compared with control mice. RNA sequencing was performed of the distal colon and choroid plexus and weighted correlation network analysis (WGCNA) was applied. Next, quantitative polymerase chain reaction (qPCR) was used for the confirmation of the expression levels of genes identified in the WGCNA analysis. The number of microglia and their morphology were assessed by Iba1 immunofluorescence in a second experiment, also including acute colitis (aDSS), which was induced by 1 week of 2% DSS, with sampling at day 7.
Results: Chronic DSS (cDSS) treatment resulted in chronic inflammation with minimal residual intestinal symptoms (control: median disease activity index (DAI) of 0 IQR [0-0], cDSS: median DAI of 0.5 [0.5-0.88], P <0.0001) after 3 weeks of recovery, which mimics quiescent IBD. At the time of sampling, the mean weight and haematological parameters (including red and white blood cells) in cDSS were comparable to those in control mice. cDSS mice exhibited significantly reduced spontaneous wheel running activity (32980 wheel rotations ± 2024.636) compared with their baseline behaviour (53976 wheel rotations ± 4233.226; P = 0.0084) and with the controls (51744 wheel rotations ± 9618.018; P = 0.0186). WGCNA on the colon and the choroid plexus expression data revealed a consensus module of 123 co-expressed genes that differed significantly between the control and cDSS mice (P = 0.00001721). These genes were implied in pathways

of neutrophil and complement activation and qPCR on different brain regions (frontal cortex, hippocampus and choroid plexus) confirmed significant upregulation of inflammatory genes Lcn2, TNFa, S100A8 and S100A9. Acute colitis was associated with activation of microglia in the prefrontal cortex compared to control mice as indicated by a significant reduction in number of branch points (aDSS: mean 30.8 ± SD 10.2, control: 48.9 ± 7.8; P = 0.0008), the branch length (aDSS: 405.9 µm ± 125.9, control: 667.5 µm ± 104.5; P = 0.0002), the number of segments (aDSS: 65.0 ± 20.5, control: 101.6 ± 15.9; P = 0.0012), the number of terminal points (aDSS: 34.2 ± 10.1, control: 53.0 ± 8.6 P = 0.0008) and the microglial volume (aDSS: 386.5 µm3 ± 127.6, control: 659.1 µm3 ± 89.9; P = 0.0001). These changes persisted in mice that recovered from chronic colitis; compared to controls a significant reduction was seen in the branch points (cDSS: 32.8 ± 5.1; P = 0.0042), branch length (cDSS: 465.3 ± 87.6 µm ; P = 0.0045), segments (cDSS: 71.2 ± 13.3; P = 0.0095), terminal points (cDSS: 37.1 ± 5.7; P = 0.0063) and microglial volume (cDSS: 428.9 ± 77.7; control: P = 0.0014).
Conclusions: In this mouse model of chronic extinguished colitis reduced spontaneous activity was seen, indicating fatigue-like behaviour as observed in patients with IBD. Moreover, mice that recovered from colitis exhibited persisting neuroinflammation.

- I11 -

DISTINCT BIOLOGICAL PROFILES ASSOCIATED WITH THE RISK OF SHORT-TERM RELAPSE AND MID/LONG-TERM RELAPSE IN CROHN'S DISEASE PATIENTS STOPPING INFLIXIMAB. N. Pierre (1), V. Huynh-Thu (2), D. Baiwir (3), G. Mazzucchelli (4), M. Fléron (3), L. Trzpiot (4), G. Eppe (4), D. Laharie (5), J. Satsangi (6), J. Colombel (7), E. Hertervig (8), M. Meuwis (1), E. Louis (9) / [1] University of Liège, Liège, Belgium, Laboratory of Translational Gastroenterology, [2] University of Liège, Liège, Belgium, Department of Electrical Engineering and Computer Science, [3] University of Liège, Liège, Belgium, GIGA Proteomics Facility, [4] University of Liège, Liège, Belgium, Laboratory of Mass Spectrometry, [5] Centre Hospitalier Universitaire de Bordeaux, Bordeaux, France, Service d'Hépato-gastroentérologie et oncologie digestive, [6] John Radcliffe Hospital, United Kingdom, Translational Gastroenterology Unit, [7] Icahn School of Medicine at Mount Sina, United States, Division of Gastroenterology, [8] Skane University Hospital, Sweden, Department of Gastroenterology, [9] Liege University Hospital, Belgium, Hepato-Gastroenterology and Digestive Oncology Department.

Introduction: In Crohn's disease (CD) patients stopping infliximab (IFX), we recently showed that the risk of short-term relapse (<6 months) and mid/long-term (>6 months) relapse were associated with distinct biological profiles (STORI trial).
Aim: To test in an independent trial (SPARE), the external validity of our previous results showing distinct biological profiles associated with the risk of short-term and mid/long-term relapse in CD patients stopping IFX.
Methods: The SPARE trial has included 211 CD patients (from 64 sites in Europe and Australia) in steroid-free remission >6 months, receiving a combined therapy (IFX and immunosuppressant (IS)) >8 months and who were then randomised in three arms: continuing combo, stopping IFX or stopping IS. The arm stopping IFX was used to externally validate our findings generated in the STORI trial. To this end, the measurement of 161 proteins obtained in the baseline serum of STORI was repeated in SPARE (arm stopping IFX) with the same technologies: selected reaction monitoring (SRM, 69 proteins measured in 67 patients) or proximity extension assay (PEA, 92 proteins measured in 63 patients). Associations between serum protein levels and time to relapse (HR: hazard ratio and its associated statistics) were determined by using univariable Cox model in the stratified (relapse <6 or >6 months) and non-stratified cohort.
Results: In STORI and SPARE, the risk of short-term relapse was associated (p-value<0.05) with a high serum level of inflammatory markers (IL6, CRP, HPR, ORM1, LRG1, HP, CP, APCS, ITIH3), complement components (C8B, C4B), blood coagulation proteins (F9, SERPIND1), markers of dendritic cells (LAMP3, CLEC4C) and a low serum level of a complement component (MASP1). In STORI and SPARE, the risk of mid/long-term relapse was associated (p-value<0.05) with a high serum level of a complement component (CFB) and a low serum level of a protease inhibitor (SERPINA4), a growth factor (FGF2), an anti-inflammatory cytokine (IL10).
Conclusions: We confirm that, after stopping IFX in CD patients, the risk of short-term and mid/long-term relapse are associated with distinct biological profiles. The risk of short-term relapse is deeply associated with residual inflammation while the biological picture depicting the risk of mid/long-term relapse seems less clear.

- I12 -

GENE NETWORKS IN POST-OPERATIVE ENDOSCOPIC RECURRENCE IN CROHN'S DISEASE: A KEY ROLE FOR FERROPTOSIS GENE GPX4. S. Verstockt (1), K. Machiels (1), J. Dehairs (2), K. Rems (1), D. Jans (3), I. De Greef (1), J. Sabino (1), M. Ferrante (1), B. Verstockt (1), S. Vermeire (1) / [1] KU Leuven - University of Leuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing (CHROMETA), [2] KU Leuven, University of Leuven, Leuven, Belgium, Department of Oncology, [3] KU Leuven, University of Leuven, Leuven, Belgium, Department of Human Genetics.

Introduction: An ileocolonic resection with ileocolonic anastomosis is often required in patients with Crohn's disease (CD). Postoperative recurrence (POR) is common, with host-luminal interactions being implicated. However, these interactions are poorly understood.
Aim: We aimed to obtain insights in the early mechanisms of POR CD focusing on sequencing-based gene networks in the mucosa.
Methods: We included 36 CD patients who underwent ileocolonic resection with ileocolonic anastomosis and collected mucosal biopsies from the neoterminal ileum 6 months after surgery. We defined POR by a Rutgeerts score ≥i2b at month 6 and compared this to complete absence of endoscopic activity (i0). All biopsies underwent single-end RNA sequencing (Illumina TruSeq Stranded mRNA). Gene co-expression network clusters were identified using weighted gene co-expression network analysis (R\WGCNA), were tested for correlation with the primary outcome POR and clinical factors, and multiple testing correction was applied (FDR<0.05). Cellular deconvolution was performed using xCell; and top enriched pathways and upstream regulators were analysed using IPA (p<0.05).
Results: WGCNA analysis identified 25 co-expression clusters, of which five correlated with the postoperative outcome (clusters V, VI, IX, XV, XXV). All but cluster XXV were upregulated in POR, with a profound immune-related enrichment in cluster V and VI (eg. (a)granulocyte adhesion and diapedesis, and IL17 signalling); microRNA biogenesis (cluster IX) and wound healing and fibrosis signalling (cluster XV). Interestingly, one cluster (XXV) was inversely correlated with POR, and genes within this cluster were mainly involved in autophagy, ferroptosis and oxidative stress response. The main hub gene (r=0.95, FDR=8.17E-19) within this cluster XXV was GPX4 (Glutathione peroxidase 4), a negative regulator of ferroptosis. Moreover, after cellular deconvolution, we found a positive correlation between the epithelial gene enrichment signature and the expression of GPX4 (r=0.52, p=0.0011). Finally, the main upstream regulator of the genes within this cluster XXV was HNF4A, a transcription factor known to regulate ferroptotic response.
Conclusions: We identified a mucosal transcriptomic signature associated with postoperative CD recurrence. Both autophagy and ferroptosis were found to be key protective pathways for recurrence with GPX4 as central hub. Our results complement recent findings of impaired epithelial GPX4 activity in ileal CD lesions.

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A GENETIC ANALYSIS OF FAMILIAL AGGREGATION IN INFLAMMATORY BOWEL DISEASE MULTIPLEX FAMILIES. D. Jans (1), H. Lee (2), M. Ferrante (3), S. Vermeire (4), I. Cleynen (1) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Human Genetics, Laboratory for Complex Genetics, [2] University of Ulsan College of Medicine, Ulsan, Korea, Department of Biochemistry and Molecular Biology, [3] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing (CHROMETA), [4] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing (CHROMETA).

Introduction: Relatives of patients with inflammatory bowel disease (IBD) have a higher risk to develop IBD than the general population. In some families, even a remarkably high prevalence of disease is found.
Aim: Here, we aim to determine the role of the known IBD risk loci in familial aggregation of disease, as well as to study if there are common variants specific to familial IBD.
Methods: Imputed immunochip genotypes of 55 families [157 Crohn's disease (CD), 29 ulcerative colitis (UC) and 138 unaffected relatives] that have at least three affected, first-degree relatives were used. A sporadic dataset (1705 CD, 917 UC, 873 controls) was used for comparison. For each individual, a polygenic risk score (PRS) was calculated with PRSice based on the IBD summary statistics of de Lange et al (2017), a p-value threshold ≤0.01 and MAF≥0.01. The mean PRS of all relatives of one family is denoted the familial PRS. Family-based association analyses were performed with SAIGE. The significance threshold for association used was p<1e-4.
Results: As a group, unaffected relatives have a lower PRS than affected relatives (p=1.36e-5, β(se)=-0.60(0.14)), but still higher than unrelated controls (p=2.07e-4, β(se)=0.39(0.11)). Twenty-four families have a familial PRS that is higher than the mean PRS of sporadic cases, and seven families have a familial PRS that is lower than the mean PRS of unrelated controls, the low PRS families. In most families, the affected members have a higher mean PRS than the unaffected members. This relationship however is sometimes reversed, especially in the low PRS families. SAIGE found nine variants to be associated with familial IBD. Two independently associated variants, rs2241130 in IL1RL2 (p=1.19 e-5, β(se)=1.21(0.28)) and rs144641193 in IL1RL1 (p=8.23e-5, β(se)=1.29(0.33)) reside in a known IBD locus (IL18RAP). Some other identified variants were also located in genes previously implicated in IBD, either through GWAS [rs72781786 in PRKCQ (p=2.93e-5, β(se)=-0.95(0.23))], or via functional studies [rs2242601 in EPHA1 (p=1.43e-5, β(se)=0.70(0.16)) and rs2272766 in CTSB (p=5.98e-5, β(se)=0.65(0.16))]. A restricted analysis of the low PRS families identified only one significant variant: rs11579543, located between RPE65 and DEPDC1 (p=6.12e-5, β(se)=-2.71(0.68)).
Conclusions: Our analysis indicates that common risk variants play an important role in familial aggregation of disease in many multiplex families. Some families however have a very low polygenic risk, indicating shared environmental factors might be relatively more important, or genetic factors not captured by the score, e.g. rare variants, may have contributed. Also, a few loci are specifically implicated in familial IBD, some related to the immune system, e.g. CLECL1 and CD69.

IMPACT OF IMMUNOMODULATING TREATMENT MODALITIES, ACTIVE SMOKING AND (REPEATED) COVID19 VACCINATION ON S-ANTIBODY SEROCONVERSION IN IMID PATIENTS. RESULTS OF THE BELCOMID STUDY: BELGIAN COHORT STUDY OF COVID-19 IN IMMUNE MEDIATED INFLAMMATORY DISEASES (IMID). J. Geldof (1), M. Truyens (1), J. Sabino (2), M. Ferrante (2), J. Lambert (3), H. Lapeere (3), T. Hillary (4), A. Van Laethem (4), K. de Vlam (5), P. Verschueren (5), E. Padalko (6), T. Lobaton (7), S. Vermeire (2) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology and Hepatology, [2] University Hospitals Leuven, Belgium, Department of Gastroenterology and Hepatology - Translational Research in Gastrointestinal Disorders (TARGID), Department of Chronic Diseases and Metabolism (CHROMETA), [3] University Hospital Ghent (UZ Gent), Gent, Belgium, Department of Dermatology, [4] University Hospitals Leuven, Belgium, Department of Dermatology, [5] University Hospitals Leuven, Belgium, Department of Rheumatology, [6] University Hospital Ghent (UZ Gent), Gent, Belgium, Department of Laboratory Medicine, Department of Diagnostic Sciences, [7] University Hospital Ghent (UZ Gent), Gent, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Targeted Immune-Modulating Therapies (TIMT) and immunomodulators (IMM) for Immune Mediated Inflammatory diseases (IMID) theoretically interfere with humoral responses against COVID19. However, IMID patients and particularly patients receiving immunosuppressive treatment were excluded from phase-3 COVID19 vaccination efficacy trials. Real-world observational data is therefore required to provide more insight into the efficacy of COVID19 vaccination in IMID patients.
Aim: To explore the interaction between IMIDs, immune-modulating treatment modalities and SARS-CoV-2 infection and vaccination in a real-life patient cohort.
Methods: A multidisciplinary, prospective observational cohort study was set up at two university hospitals. Consecutive patients seen between 17/12/2020 and 28/02/2021 during routine follow-up for IMIDs of the gut, joints and skin were invited to participate. Patient data and serological samples were collected at 3 predefined periods: before the national vaccination campaign (17/12/2020-28/02/2021), after start of the vaccination campaign but before booster vaccination (01/07/2021-24/09/2021), after booster vaccination (03/01/2022-15/03/2022). Spike(S) protein antibodies were analysed with the AbbottArchitectTM assay. R v4.0.2 was used for analyses.
Results: At inclusion period 2, 2065 patients participated. 1547 patients (64% IBD, 20% rheumatologic IMID, 16% dermatologic IMID) had received complete baseline vaccination (2 doses mRNA-1273, BNT162b2, ChadOx1 nCoV-19 or 1 dose JN78436735). The majority was treated for their IMID with TIMT (79.8%). In 12.7% TIMT was combined with an IMM. TIMT included biologics, JAKi and apremilast. IMM included methotrexate, ciclosporin, dimethyl-fumarate, mycophenolate mofetil, leflunomide, hydroxychloroquine and thiopurines. S-antibody seroconversion rate in patients with complete baseline vaccination was 91.2%. At period 3, 1169 patients (72% IBD, 16% rheumatologic IMID, 11% dermatologic IMID) had received 1 booster (BNT162b2 or mRNA-1273) vaccination. In 84.9%, IMID treatment consisted of TIMT and in 17.1% this was combined with an IMM. S-antibody seroconversion rate in patients after 1 booster was 98.3%. One hundred and thirty patients (48% IBD, 23% rheumatological IMID, 29% dermatological IMID) had received 2 boosters at period 3. Although 82.3% was on TIMT and 13.8% on combined TIMT+IMM, S-antibody seroconversion rate in this group was 100%. At period 3, 37 patients had refused all vaccinations. Only one of these patients was not on TIMT or IMM treatment. No S-antibody seroconversion was found in 15, although 23 patients previously experienced confirmed COVID19. Logistic regression analyses revealed a significantly higher odds of no S-antibody seroconversion at both inclusion periods in IMID patients treated with IMM (p2: OR1.75, 95%CI 1.07-2.81, P=0.022 – p3: OR2.96, 95%CI 1.29-6.51, P=0.0083), combination IMM+TIMT (p2: OR2.86, 95%CI 1.78-4.54, P<0.001 – p3: OR4.63, 95%CI 2.16-9.69, P<0.001) or systemic steroids (p2: OR2.88, 95%CI 1.57-5.08, P<0.001 – p3: OR13.7, 95%CI 4.94-36.0, P<0.001). Univariate analyses showed higher risk of S-seronegativity in active smokers in period 3 (RR2.5, 95%CI1.4-4.4, P=0.003) and a higher risk of being in the lowest S-antibody titre quartile (p2: RR1.4, 95%CI 1.2-1.7, P=0.002 – p3: RR1.5, 95%CI 1.2-1.8, P<0.001). TIMT monotherapy did not influence seroconversion rates at inclusion period 3 (p2: OR1.87, 95%CI 1.07-3.50, P=0.038 – p3: OR2.19, 95%CI 0.75-9.35, P=0.21) but was associated with higher odds of the lowest S-antibody titre quartile (OR2.34, 95%CI 1.56-3.62, P<0.001). Among TIMT options, rituximab had higher odds of S-seronegativity (p2: OR14.6, 95%CI 4.80-48.2, P<0.001 – p3: OR25.3, 95%CI 6.35-106, P<0.001).
Conclusions: The S-antibody seroconversion rate in this real-life IMID population was high after baseline vaccination and increased further proportionally with booster vaccination, highlighting the value of repeated vaccination. However, the serologic response may be blunted due to different IMID treatment modalities and smoking.

A TRANSCRIPTOMIC SIGNATURE SCORE TO PREDICT DYSPLASIA AND COLITIS-ASSOCIATED COLORECTAL CANCER IN INFLAMMATORY BOWEL DISEASE PATIENTS. A. Cremer (1), N. Rosewick (2), E. Trépo (1), F. Libert (3), P. Demetter (4), M. De Vos (5), J. Rahier (6), F. Baert (7), T. Moreels (8), E. Macken (9), E. Louis (10), S. Vermeire (11), D. Franchimont (1) / [1] Erasme Hospital, Brussels, Belgium, Gastroenterology, [2]

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Introduction: Inflammatory bowel disease (IBD) (Crohn's disease (CD) and ulcerative colitis (UC)) is associated with a higher risk of developing colorectal cancer (CRC), according to the inflammation-dysplasia-cancer (IDC) sequence from inflammation, to indefinite, low-grade (LGD), high-grade dysplasia (HGD), and colitis-associated colorectal cancer (CAC).
Aim: Our objective was to identify the differential gene expression between these mucosal neoplastic alterations and provide a transcriptomic gene signature associated with the IDC sequence.
Methods: This is a national cohort study conducted across 7 Belgian tertiary centers that retrospectively evaluated all patients with histologically confirmed IBD, diagnosed with at least 1 episode of dysplasia (LGD or HGD) and/or CAC between January 1, 1990, and December 31, 2016. Two cohorts of patients were analyzed: a transversal cohort of patients who presented during their follow-up with only one type of lesions (LGD, HGD or CAC), and a longitudinal cohort of patients who presented at least 2 types of lesions (LGD, HGD and/or CAC) during their follow-up. RNA-seq was performed from formalin-fixed paraffin-embedded (FFPE) samples. We followed an ordinal logistic regression (olm) method to screen for significant IDC sequence-associated genes that could be used as predictive biomarkers for early cancer detection. We then incrementally took the top N genes ordered by olm regression p-values and computed the transcriptomic signature score for each samples using this list of top N genes.
Results: 362 FFPE samples were selected histopathologically of which 196 underwent RNA sequencing. Of those, a total of 135 samples passed quality control. Principal component analysis and unsupervised clustering on 1% (363 genes) of the most variable genes from 36,238 genes and 135 samples was performed on RNA-seq data and showed an overall good clustering between the 4 groups of IBD-IDC sequence (normal controls, inflamed controls (colonic biopsies from endoscopically active or quiescent disease, dysplasia (LGD and HGD), and CAC). To further investigate the role of these top 1% genes, we performed a gene set enrichment analysis. Top-most enriched pathways were associated to humoral immune response, immunoglobulin complex and antigen binding reflecting an overall role of these genes in immune response. In our transversal cohort, a gene signature of 19 genes that correlated with disease grade (Normal controls → inflamed controls→ LGD/HGD → CAC) was identified using ordinal logistic regression. Among these 19 genes, 16 were upregulated and 3 were downregulated. Heatmap showed that groups were clustered together and very well separated from each other when considering only the 19 genes of the gene signature. Based on the 19 genes expression, we build a transcriptomic signature score to predict dysplasia (LGD and HGD) and CAC in IBD patients. The overall correct prediction rate of the transcriptomic signature score was 81.25% in our transversal cohort and 91.30% in the longitudinal cohort.
Conclusions: In this study we analysed the expression of 135 samples from different stages of the IDC sequence in IBD. We were able to select 19 genes based on their propension to better reflect the progression between the different groups (Normal controls → Inflamed controls → LGD/HGD → CAC). From these 19 genes, we built a transcriptomic signature score which showed a good prediction rate for dysplasia and CAC.

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DOSE-DEPENDENT HISTOLOGIC IMPROVEMENT AND ATTENUATION OF INFLAMMATION BY ENGINEERED HIGH ACETATE PRODUCING SACCHAROMYCES BOULARDII IN DSS-INDUCED COLITIS.

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Introduction: It has been hypothesized that the probiotic potential of the yeast Saccharomyces boulardii (Sb) is associated with its acetate production. This SCFA is of interest in IBD due to its cross-feeding potential with beneficial butyrate-producing bacteria and low toxicity to epithelial cells . Our previous in vitro work supports this hypothesis (Deleu et al, 2022) but still requires in vivo validation.
Aim: Therefore, we evaluated the effect of different engineered Sb strains producing variable amounts of acetate in DSS-induced colitis in mice.

Methods: Nine week old female C57/Bl6 mice (N=120) were allocated to 12 treatment groups receiving drinking water or 2.75% DSS in combination with PBS (control), Baker's yeast (non-probiotic control), SDH1 (non-acetate producing Sb), ENT (transient acetate producing Enterol strain-probiotic control), SbP (high acetate producing Sb) and ENT3 (extra high acetate producing Sb). Disease activity including weight loss, diarrhoea and the presence of occult blood was scored daily. On day 7, the DSS groups were transferred to regular drinking water and on day 14 mice were sacrificed. Colonic tissue and blood were collected for resp. histologic and cytokine analysis.
Results: Disease activity, determined by the area under the curve, in DSS subgroups was lower for SbP compared to PBS and Baker's yeast (both $p<0.05$). Remarkably, Sb SDH1 showed even higher disease activity compared to the Sb strains ENT, SbP and ENT3 (all $p<0.05$). At sacrifice, macroscopic damage score in DSS subgroups was lower for SbP and ENT3 (both $p<0.05$) compared to Sb SDH1 and the colon weight/length-ratio was decreased for ENT and SbP compared to Sb SDH1 (resp. $p=0.06$ and $p=0.08$). Higher histologic inflammation was noted in the non- or only transient-acetate producing strains on DSS compared to healthy PBS control (all $p<0.05$), whereas this increase was not observed for both high-acetate producing strains SbP and ENT3 on DSS (p=NS). Lower IL1β, IL2 and IL4 concentrations for DSS groups on SbP and ENT3 compared to DSS groups on Sb SDH1 and ENT were observed (all $p<0.05$). In contrast, IL10, TNFα and KC/GRO were lower for the DSS groups on Sb SDH1 and ENT compared to DSS groups on SbP, ENT3, and even PBS for IL2 and 4 (all $p<0.05$).
Conclusions: Engineered high acetate producing Sb strains show a significant trend towards improved attenuation of DSS-induced colitis compared to the parent Sb strain on disease activity, macroscopical damage score and show production-dependent response on histology. Mixed pro-inflammatory serum profiles were observed potentially pointing in the direction of other effects of acetate accumulation. Together with our previous in vitro work, these data indicate a role for Sb-produced acetate in attenuating inflammation.

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NEGATIVE IMPACT OF HIGH BODY MASS INDEX ON THE EFFICACY OF ANTI-TNFA AGENTS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE. F. Hamoir (1), F. De Leuze (1), M. Denis (1), B. De Vroey (1), N. De Suray (1), G. Burnet (1), H. Piessevaux (1), O. Dewit (1) / [1] Saint-Luc University Hospital, Brussel, Belgium, Gastroenterology.

Introduction: Anti-tumour necrosis factor (TNF)-α agents are a therapy of choice in the induction and maintenance treatment of inflammatory bowel disease (IBD). Unfortunately, their efficacy varies. Some IBD patients are primary non-responders and many will experience a secondary loss of response. However, we do not yet have good predictors of their efficacy. Obesity, which prevalence increases worldwide, is also increasingly found in IBD population. Some studies suggest an association between obesity and poorer response to anti-TNFα therapy in IBD patients, although with conflicting results.
Aim: The aim of this study is to assess the impact of patients' body mass index (BMI) on the efficacy of anti-TNFα agents in IBD and if there is difference according to the route of administration (intravenous (IV) vs subcutaneous (SC)) or the type of disease (Crohn's disease (CD) vs ulcerative colitis (UC)).
Methods: We retrospectively collected data from 188 patients with IBD, aged ≥ 18 years, treated with a first anti-TNFα agent started exclusively in our center between January 2002 and December 2020 to avoid missing data. A lack of response or loss of response to anti-TNFα therapy was defined by the need to optimize or change the treatment or by the initiation of any intercurrent treatment (steroid therapy, hospitalization, or surgery). The frequency of the event and the time to its occurrence were analyzed and compared according to BMI using uni- and multivariate logistic regression models with the use of survival curves (Kaplan-Meier), represented by BMI categories (<18.5; 18.5-25; 25-30 and obesity ≥ 30 kg/m²).
Results: In this cohort of 188 patients (143 CD, 43 UC, 2 Indeterminate Colitis), 8% were obese. We observed that the higher the patient's BMI, the earlier the risk of optimization or change of treatment (HR=1.043, p=0.045). Association was even stronger for obese patients (HR=2.13, p=0.018). After adjustment for IBD type and route of administration, association with obesity persisted. Two other characteristics - female gender (HR=1.56, p=0.012) and higher CRP (HR=1.14, p=0.021) – were associated with earlier optimization or change of treatment. Similarly, analysis of survival curves showed a significant difference in time to optimization or change of treatment between BMI categories in patients with CD (p=0.02) but not in those with UC (p=0.87). No association was found between BMI and need for intercurrent treatment.
Conclusions: This study confirms an association between higher BMI – specifically obesity - and an earlier loss of efficacy of a first anti-TNFα treatment, regardless of IBD type or route of drug administration. This observation confirms the need for specific management of obese patients with IBD. Prospective studies with analysis of drug trough levels are required for a better understanding of the mechanisms involved in the response to anti-TNFα therapy in IBD obese patient.

IMPACT OF DIFFERENT TYPES OF PHYSICAL ACTIVITY IN INFLAMMATORY BOWEL DISEASE. A. Gofflot (1), L. Monin (2), L. Seidel (3), C. Reenaers (2), S. Kropp (2), C. Van Kemseke (2), P. Latour (2), B. Forthomme (4), J. Croisier (4), E. Louis (2), S. Vieujean (2) / [1] University of Liège, Liège, Belgium, Motricity Sciences, [2] University Hospital CHU of Liège, Belgium, Hepato-Gastroenterology and Digestive Oncology, [3] University Hospital CHU of Liège, Belgium, Department of Biostatistics and Medico-economic Information,, [4] University Hospital CHU of Liège, Belgium, Department of Physical Medicine and Rehabilitation.

Introduction: Moderate physical activity (PA) appears to be beneficial for inflammatory bowel disease (IBD), improving the symptoms of the disease and promoting the maintenance of remission. However, little is known about the impact of different types of PA on IBD activity.
Aim: The objective of this study was to define the impact of different types of physical activity in IBD patients.
Methods: IBD patients with stable treatment without steroids for 4 months were prospectively included and randomized into 3 groups: muscle strengthening exercises, aerobic exercises, and a control group. The impact of a 10-week training period with 2 sessions per week was evaluated. Following parameters were collected: clinical activity of the disease (Mayo score for ulcerative colitis or UC, Harvey-Bradshaw index or HBI for Crohn's disease or CD, patient reported outcome or PRO for both), Godin Leisure Time Exercise Questionnaire or GLTEQ (assessing PA level), Metabolic Equivalent Task or MET (assessing sedentarity level), barriers to PA, quality of life assessment (by EuroQol 5 dimensions or EQ5D and Short health scale or SHS), Inflammatory Bowel Disease Fatigue (IBD-F), physical abilities according to exercise stress test and maximum strength test.
Results: Between January 2021 and September 2022, a total 33 patients were enrolled in the program. Of these, 24 patients (13 women, 17 CD, median age of 31.6 [IQR, 29.4- 46.4]) completed the program and were included in the analysis (dropout rate of 18.2%). Table 1 shows the characteristics of these patients at inclusion. Eight, six and ten patients were respectively randomized in the muscle strengthening, aerobic exercise and control groups. After the training period, 50% of patients in the muscle strengthening group and 66.7% of patients in the aerobic exercise group showed a clinical improvement (according Mayo score and HBI). Strengthening was associated with significant reduction in PRO rectal bleeding in UC patients ($p<0.0001$) and aerobic exercise was associated with a significant lowering of HBI ($p=0.039$). Among the 24 patients, 2 CD patients relapsed in the muscle strengthening group during the training period. Aerobic exercise significantly reduced the barriers to PA ($p=0.037$). In neither group did we find any positive or negative impact of PA on quality of life or fatigue. Strengthening exercise and aerobic exercise significantly improved VO2max (maximal oxygen consumption) and Pmax in the exercise stress test, respectively. Most of the maximum strength tests were improved in the muscle strengthening group.
Conclusions: PA was well tolerated and associated with an improvement of disease activity in the majority of the IBD patients. There may be a variable impact of different types of PA in CD and UC, which should be explored further in larger cohorts.

INFLUENCE OF SARCOPENIA ON PERIOPERATIVE MANAGEMENT AND POSTOPERATIVE OUTCOME IN PATIENTS WITH CROHN'S DISEASE UNDERGOING INTESTINAL SURGERY: A RETROSPECTIVE STUDY. C. O'Neill (1), S. Haenen (2), W. Coudyzer (3), G. Bislenghi (4), A. D'Hoore (4), B. Verstockt (5), M. Ferrante (5), S. Vermeire (5), J. Sabino (5) / [1] University Hospitals Leuven, Belgium, Gastroenterology and Hepatology, [2] Regionaal ziekenhuis Heilig Hart Leuven, Leuven, Belgium, Gastroenterology and Hepatology, [3] University Hospitals Leuven, KU Leuven, Belgium, Department of Radiology, [4] University Hospitals Leuven, KU Leuven, Belgium, Department of Abdominal Surgery, [5] University Hospitals Leuven, KU Leuven, Belgium, Department of Gastroenterology and Hepatology & Department of Chronic Diseases and Metabolism CHROMETA- Translational Research in GI disorders.

Introduction: Sarcopenia (loss of skeletal muscle mass and/or strength) is a predictor of postoperative morbidity in various surgical populations.
Aim: We evaluated the impact of sarcopenia in postoperative outcomes after intestinal surgery in patients with Crohn's disease (CD) at a tertiary referral centre.
Methods: This is a retrospective analysis of all patients with CD undergoing intestinal surgery at our centre, between January 2013 and September 2019 with available abdominal computed tomography images within 90 days of surgery. The images were assessed for sarcopenia according EWGSOP2 criteria (Skeletal Muscle Index <39 cm2/m2 for female and <55 cm2/m2 for male) and visceral and subcutaneous fat areas. All patients were coded for postoperative complications using the Clavien–Dindo classification.
Results: A total of 114 patients with Crohn's disease were included. The prevalence of sarcopenia was 67.5%. Common intestinal procedures were ileocecal resections (49%), segmental small-bowel resections/stricturoplasty (6.1%), and colon resection (8.8%). Major postoperative complications (Clavien-Dindo >=3) were observed in 17 patients (14.9%). Sarcopenic patients have more frequently penetrating phenotype than patients without sarcopenia ($p=0.007$).

Body mass index (BMI) and serum albumin levels were significantly lower ($p<0.001$ and $p=<0.037$, respectively) and C-reactive protein levels were significantly higher ($p=0.014$) in sarcopenic patients compared to non-sarcopenic patients. Furthermore, both visceral and subcutaneous fat were significantly lower (both $p<0.001$) in patients with sarcopenia. ICU admission, rates of postoperative complications within 30 days, infections, reoperation and re-hospitalization were not significantly different between sarcopenia and non-sarcopenia groups. However, there was a trend of a longer length of hospital stay ($p= 0.062$) in patients with sarcopenia. Sarcopenic patients received significantly more preoperative and postoperative parenteral nutrition ($p=0.006$ and $p=0.035$, respectively) and protective ileostomy ($p=0.025$) compared with patients without sarcopenia.
Conclusions: The prevalence of sarcopenia based on EWGSOP2 criteria is high in patients with CD requiring bowel resection. In this cohort, sarcopenia was not linked to higher rate of postoperative complications, although this might be explained by different surgical procedures and nutrition management before and after surgery for CD.

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LARGE PORTION OF PATIENTS WITH INFLAMMATORY BOWEL DISEASES REPORT DIFFICULTIES WITH PSYCHOLOGICAL WELLBEING, EVEN IN ABSENCE OF DISEASE ACTIVITY. B. Keersmaekers (1), M. Lenfant (2), I. van den Eijnden (3), A. Teugels (4), J. Pedro Guedelha Sabino (2), B. Verstockt (2), S. Vermeire (2), I. Van Diest (4), M. Ferrante (2) / [1] University Hospitals Leuven, , Belgium, Gastroenterology and Hepatology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [3] KUL - University of Leuven, Leuven, Belgium, Biomedical Sciences, [4] KU Leuven - University of Leuven, Leuven, Belgium, Research Group Health Psychology.

Introduction: The mental health status of patients with inflammatory bowel diseases (IBD) is rarely assessed in daily clinical practice. Therefore, many patients fail to receive the psychological care needed.
Aim: We measured the prevalence of psychological symptoms and impact on quality of life (QoL) in our IBD population and identified risk factors associated with decreased psychological wellbeing.
Methods: All Dutch speaking patients with Crohn's disease (CD) or ulcerative colitis (UC) treated at our tertiary referral center received an electronic survey of five validated questionnaires, including the Health Monitor (evaluating perceived control and disease acceptance), the Hospital Anxiety and Depression Scale (HADS), the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F, evaluating fatigue), the IBD disability index (IBD Disk) and the Visceral Sensitivity index (VSI). Previously established cut-off scores were used for each questionnaire to assess more severe patient-reported outcome (Table 1). To measure clinical disease activity both the two-component patient-reported outcomes (PRO-2) and Manitoba IBD Index (MIBDI) were used.
Results: Out of the 4352 patients (51.8% female, median [range] age 48 [18-98] years, 64.2% CD) who received the digital version of the questionnaire, 988 respondents were included for analysis (22.7% participation rate, 53.5% female, 51 [18-94] years, 61.6% CD, 31.5% with active disease).In total, 52.9% reported low perceived control and low disease acceptance (Health Monitor segment IV). Furthermore, 34.8% and 13.2% reported symptoms of, respectively, anxiety and depression. Additionally, 35.0% reported high fatigue, 33.2% reported severe IBD-related disability and 76.5% reported high visceral sensitivity. As expected, disease activity was associated with lower QoL and psychological wellbeing . However, 14.2% of UC and 46.6% of CD patients who did not report disease activity were also included in segment IV (low perceived control and disease acceptance). In general, patients with CD reported a lower perceived control and lower disease acceptance, more visceral sensitivity, more fatigue , more symptoms of anxiety and depression compared to patients with UC. Female patients reported greater IBD-related disability, lower perceived control and lower disease acceptance, more symptoms indicative of anxiety, more visceral sensitivity and more fatigue.
Conclusions: Despite the known limitation of participation bias in questionnaires, these results suggest that a large portion of patients with IBD have difficulties with their psychological wellbeing. Patients with active disease, CD patients and female patients are the main subgroups that are at risk for decreased psychological wellbeing. These results can help to optimize future psychological support programs in the IBD population.

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ASSESSMENT OF THERAPEUTIC RESPONSE IN CROHN'S DISEASE BY DYNAMIC CONTRAST ENHANCED MRI. S. Vieujean (1), R. Gillard (2), F. Calvaer (2), M. Chayeb (2), L. Seidel (3), C. Reenaers (1), S. Kropp (1), C. Van Kemseke (1), P. Latour (1), E. Louis (1), P. Meunier (2) / [1] CHU of Liège, Belgium, Hepato-Gastroenterology and Digestive Oncology, [2] CHU of Liège, Belgium, Department of Radiology, [3] CHU of Liège, Belgium, Department of Biostatistics and Medico-economic Information.

Introduction: In a previous study comparing dynamic contrast-enhanced (DCE)-MRI parameters in affected and unaffected segments of Crohn's disease (CD) patients with those of a control group, we found significantly lower perfusion parameters in unaffected segment of CD patients compared to the unaffected ones of control subjects (1). This led us to consider 2 hypotheses: either there is a constitutional perfusion disorder in CD patients, or it reflects a dynamic

disequilibrium between affected and unaffected segments in patients with active disease (and a blood flow diversion to the affected segments). In this latter case, this perfusion parameter in unaffected segment could represent a good indirect marker of disease activity.
Aim: To distinguish between these two hypotheses, we aimed to assess the perfusional parameters changes in affected and unaffected segments of patients with active disease before after 3 months of treatment.
Methods: In this single-center prospective study, we performed a DCE-MRI in relapsing CD patients for whom a treatment change was required (T0), as well as, at the end of induction. Regions of interest were drawn in affected and unaffected segments and the program (Olea Medical - Canon) provided values for transfer constant (Ktrans), fractional volume of extravascular-extracellular space (Ve), slope of enhancement (SoE), time to maximum enhancement (TME), maximum enhancement (ME) and enhancement ratio (ER) which were determined and compared. The following clinical data were also collected: gender, age, disease duration, Montreal classification, previous surgery, smoking habits, previous IBD treatment, Harvey Bradshaw Index (HBI), c-reactive protein (CRP) and faecal calprotectin (both obtained within a 3-month time window from the MRI). Response to treatment was defined as HBI less than 4 with CRP less than 5 and fecal calprotectin less than 250 µg/g.
Results: A total of 30 CD patients (16 men, mean age ± SD : 40.9 ± 14.3) were included between March 2020 and March 2022. Of these 30 patients, 16 patients underwent MRI before and after 3 months of treatment allowing paired comparisons. Comparisons of affected and unaffected segments in 30 CD patients showed a significant increase of all perfusional parameters in affected segments compared to unaffected, except for TME. Regarding the association with biomarkers, there was a significant negative relationship between KTrans mean and CRP (r=-0.44, p=0.039). We did not observe any significant change in paired comparison after treatment in affected and unaffected segments, including when considering only patients who responded at 3 months.
Conclusions: We did not observe any significant changes in MRI perfusion parameters after medical treatment in CD. This probably reflects a slower change of MRI perfusional parameters compared to clinical of biochemical parameters. These MRI perfusional parameters are thus not appropriate as objective markers of short term response but should be re-examined on the longer term. (1) Vieujean S, et al. Magnetic resonance enterography perfusion parameters reveal complex changes in affected and unaffected segments in Crohn's disease. Scand J Gastroenterol. 2020

- I22 -

PATTERNS OF CORTICOSTEROID EXPOSURE AND EXCESS IN INFLAMMATORY BOWEL DISEASE: RESULTS FROM THE DETERMINANTS, INCIDENCE AND CONSEQUENCES OF CORTICOSTEROID EXCESS (DICE) ONLINE MONITORING TOOL. E. Louis (1), J. Wye (2), S. Nancey (3), I. Blumenstein (4), R. Barkan (5), W. Fries (6), F. Gomollón (7), A. Çelik (8), C. Selinger (9), G. Parkes (10), T. Finney-Hayward (11), T. Raine (12) / [1] University Hospital CHU of Liège, Belgium, Department of Gastroenterology, [2] Addenbrooke's Hospital, Cambridge, United Kingdom, Gastroenterology, [3] Hospices Civils de Lyon, Lyon, France, Service d'hépatogastroentérologie, [4] JW Goethe University Hospital, Frankfurt, Germany, Gastroenterologie und Hepatologie, [5] Rabin Medical Center, Petah Tikva, Israel, Gastroenterology, [6] University of Messina, Messina , Italy, Dipartimento di Medicina Clinica e Sperimentale, [7] Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain, Departamento de Medicina, Psiquiatría y Dermagología, [8] Cerraphasa Medical School, Istanbul, Turkey, Gastroenteroloji-(Hepatoloji), [9] Leeds Gastroenterology Institute, Leeds, United Kingdom, Gastroenterology, [10] The Royal London Hospital, Barts Health NHS Trust, United Kingdom, Gastroenterology, [11] AbbVie Ltd, Berkshire, United Kingdom, Medical Affairs, [12] Addenbrooke's Hospital, Cambridge, United Kingdom, Department of Gastroenterology.

Introduction: Corticosteroids (CS) play an important role in inducing a response in inflammatory bowel disease (IBD), but have a limited role as maintenance therapy due to substantial side effects.1 Despite the availability of alternative treatments and recommendations for steroid-sparing strategies in guidelines,1–3 CS dependency and excess remain common. Therefore, there is a need to quantify CS exposure and evaluate factors contributing to excess use.
Aim: This was a multi-country, cross-sectional, prospective study aimed at quantifying the incidence of CS use in patients with IBD using a bespoke online CS monitoring tool.
Methods: Each centre also completed a service-level questionnaire. Patients were included if they were ≥18 years old and had IBD for >1 year. Outcomes assessed were CS exposure within the last 12 months, and CS excess (defined as >1 course or use for ≥3 months within the last 12 months, or an inability to reduce CS below the equivalent of prednisolone 10 mg/day or budesonide 3 mg/day within 3 months of starting CS without IBD recurrence, or relapse within 3 months of stopping CS). Odds ratios (ORs) for explanatory variables were calculated using single variable then mixed effects multivariate logistic regression.
Results: Data were analysed from 2,618 patients in 44 centers in seven countries (Crohn's disease [CD], n=1,453; ulcerative colitis [UC], n=1,133; IBD-unclassified, n=32). Overall, 27.9% of patients were exposed to CS and 20.3% had excess use. Rates of CS exposure and excess were highest in patients with moderate/severe UC (66.9% and 53.5%, respectively); these patients were more likely to have had CS exposure and excess vs patients with quiescent/mild UC or CD. The probability of CS exposure and excess generally increased with the number of previous immunosuppressant/targeted therapies for CD, but not UC. CS exposure and excess were generally less likely in tertiary/academic centers

(vs community hospitals or private practice) with IBD multidisciplinary teams or dedicated clinics. In the multivariate analysis, disease severity contributed significantly to CS exposure and excess in patients with CD (OR: 2.73 and 3.16, respectively; both $p<0.001$) and UC (OR: 5.37 and 5.27, respectively; both $p<0.001$). Anti-tumour necrosis factor (anti-TNF) therapy was a significant protective factor against CS exposure and excess (OR: 0.53 and 0.50, respectively; both $p<0.001$) in CD, but not UC. Use of interleukin (IL)-12/-23 antagonists was also a significant protective factor against CS exposure (OR: 0.53; $p<0.02$) and excess (OR: 0.51; $p<0.03$) in CD but not UC. All other factors in the univariate analysis were non-significant when assessed in the multivariate analysis.
Conclusions: Corticosteroid exposure and excess remain common for patients with IBD across healthcare settings. Several factors may underlie this. In the present study, disease severity (moderate/severe vs mild/quiescent) was associated with an increased risk of CS exposure and excess in patients with CD and UC, and use of anti-TNF therapy or IL-12/-23 antagonists were associated with a decreased risk of CS exposure and excess in CD (but not UC), in the multivariate analysis.

- I23 -

CHANGE IN FATIGUE IN PATIENTS WITH ULCERATIVE COLITIS OR CROHN'S DISEASE INITIATING VEDOLIZUMAB OR OTHER BIOLOGIC THERAPY: DATA FROM BELGIAN REGISTRY PATIENTS. E. Louis (1), P. Bossuyt (2), A. Colard (3), P. Caenepeel (4), F. Baert (5), A. Hantson (6), G. Van Gassen (6), J. Zhou (7), S. Vermeire (8) / [1] CHU of Liège, Belgium, Gastroenterology, [2] Imelda Hospital, Bonheiden, Belgium, Gastroenterology, [3] Clinique MontLégia - CHC Groupe Santé, Liège, Belgium, Gastroenterology, [4] Ziekenhuis Oost Limbug (ZOL), Genk, Belgium, Gastroenterology, [5] AZ Delta, Roeselare, Belgium, Gastroenterology, [6] Takeda Belgium, Brussels, Belgium, Medical Affairs, [7] Takeda Belgium, Brussels, Belgium, Safety Statistics, [8] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology.

Introduction: Fatigue in patients (pts) with ulcerative colitis (UC) and Crohn's disease (CD) is associated with decreased quality of life.
Aim: This analysis aimed to describe fatigue evolution and identify factors associated with time to fatigue disappearance or fatigue persistence at 1 year among pts initiating vedolizumab (VDZ) or other biologic treatment (tx).
Methods: Post-hoc analysis of fatigue registry data of Belgian pts being followed in a prospective real-world safety study (PASS; NCT02674308). Pts ≥18 years with UC or CD initiating VDZ or other biologics with no prior VDZ exposure were included. Pts completed the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) and physicians collected disease characteristics at baseline and 6-month intervals (4.5-year follow-up). Fatigue persistence was defined by 2 consecutive FACIT-F scores of <40, and fatigue disappearance (in pts with baseline fatigue) by a FACIT-F score of >40. Factors associated with time to fatigue disappearance and fatigue persistence at 1 year were assessed using multivariate regression.
Results: This analysis included 465 pts with UC (n=174) or CD (n=291) who initiated VDZ (n=259) or other biologic tx (n=206) at registry enrolment (Table 1 for baseline characteristics). Change in FACIT-F scores among all pts (Figure 1) showed an improvement in fatigue in the first 6-months following tx initiation before stabilising for the remainder of the study. The Kaplan-Meier estimate for time to fatigue disappearance (Figure 2) indicated fatigue disappearance occurred in 2.1%, 6.2% and 14.2% of pts with baseline fatigue at 6, 12 and 24-months respectively. In pts with baseline fatigue, lower likelihood of fatigue persistence was associated with achieving clinical remission (OR 0.31 [0.16, 0.60]). Probability of fatigue disappearance per unit of time was estimated to be higher in pts with UC vs CD (HR 1.53 [1.07, 2.21]) and in pts achieving vs not achieving clinical remission (HR 2.02 [1.18, 3.48]) and lower in pts with vs without extra-intestinal manifestations at baseline (HR 0.62 [0.39, 0.99]). No associations were observed between fatigue persistence/disappearance and tx group, demographics, disease duration, tx history, use of other medication, history of or active fistula, IBD surgery or clinical response.
Conclusions: These real-world findings suggest fatigue in pts initiating VDZ or other biologic therapy for UC or CD improves in the first 6 months of treatment before stabilising over time. Clinical remission was associated with a lower likelihood of fatigue persistence and shorter time to fatigue disappearance.

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INFLAMMATORY BOWEL DISEASE MEETS FERTILITY: A PHYSICIAN AND PATIENT SURVEY. S. Vieujean (1), M. De Vos (2), F. D'Amico (3), K. Paridaens (4), G. Daftary (5), L. Peyrin-Biroulet (6), S. Danese (3) / [1] University Hospital CHU of Liège, Belgium, Hepato-Gastroenterology and Digestive Oncology, [2] UZ Brussel, Belgium, Centre for Reproductive Medicine, [3] IRCCS San Raffaele Hospital and Vita-Salute San Raffaele University, Italy, Department of Gastroenterology and Endoscopy, [4] Ferring International Center S.A, Switzerland, Ferring International Center S.A, [5] International PharmaScience Center, Denmark, Ferring Pharmaceuticals A/S, [6] University of Lorraine, CHRU-Nancy, France, Department of Gastroenterology.

Introduction: Inflammatory bowel diseases (IBD) affect patients during their childbearing years. Literature evidence is scarce regarding the level of knowledge among health care professionals (HCPs) and patients out the impact of IBD on fertility.
Aim: The aim of this survey was to investigate HCPs' and patients' knowledge on fertility, pregnancy, and sexual function, to evaluate how HCPs approach this topic and to report patients' reproductive outcomes.
Methods: Subjects were invited to anonymously complete an online questionnaire collecting data on demographics, patients' disease characteristics, Crohn's and colitis pregnancy-specific disease-related knowledge (CCPKnow), family planning, reason of childlessness, pregnancy outcomes, need for assisted reproductive technology, impact on sexual function, and availability of patients' information regarding IBD and pregnancy.
Results: A total of 257 HCPs from 40 countries and 793 patients (615 females, 176 males and 2 who preferred not to disclose their gender; 396 (50%) with ulcerative colitis, 381 (48%) with Crohn's disease, 14 (1.8%) with undetermined IBD) from 4 countries completed the survey. In total, 98.4% of HCPs had good or very good pregnancy-specific knowledge according to CCPKnow score, compared to only 29.3% of patients. Of the women surveyed, 56.3% had no children (14.1% due to a voluntary choice). A total of 427 pregnancies and 401 live births were reported in 266 women. Twenty-four pregnancies (5.6%) in 22 women required assisted reproductive technologies (ART). There were no more complications in pregnancies resulting from ART compared with spontaneous conception (5/24; 20.8% vs 211/401; 52.6%). Three quarters of IBD patients (75.6%) had breastfed. An impaired sexual function was found in one-fifth (21.9%) of men with IBD, while two-thirds (66.1%) of the women reported sexual function impairment. Surprisingly, 63% of patients reported not having received any information about IBD and pregnancy, and only 10% of patients had received information from their IBD specialist. In addition, 42.1% and 36% of HCPs had already referred a patients to a medically assisted reproduction centre to receive general information about their reproductive health and about options of fertility preservation (e.g., cryopreservation), respectively.
Conclusions: IBD patients have a poor knowledge about the impact of IBD on fertility and pregnancy and HCPs does not sufficiently inform their patients. More information on these topics is needed for IBD patients.

- I25 -

EFFICACY AND SAFETY OF UPADACITINIB IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS RECEIVING 16 WEEKS' EXTENDED INDUCTION TREATMENT FOLLOWED BY 52 WEEKS' MAINTENANCE TREATMENT IN THE U-ACHIEVE/U-ACCOMPLISH TRIALS. R. Panaccione (1), S. Danese (2), W. Zhou (3), J. Klaff (4), D. Ilo (5), X. Yao (3), G. Levy (5), P. Doyle Higgins (6), E.V. Loftus, Jr (7), S. Vermeire (8) / [1] University of Calgary, Calgary, Canada, Inflammatory Bowel Disease Group, [2] IRCCS San Raffaele Hospital and Vita-Salute San Raffaele University, Italy, Gastroenterology and Gastrointestinal Endoscopy Unit, [3] Abbvie Inc., Chicago, United States, Statistics, [4] Abbvie Inc., Chicago, United States, Clinical Development Immunology, [5] Abbvie Inc., Chicago, United States, Medical Affairs, [6] University of Michigan, Ann Arbor, United States, Gastroenterology Clinic, [7] Mayo Clinic, Rochester, United States, Gastroenterology and Hepatology, [8] University Hospitals Leuven, Belgium, Gastroenterology and hepatology.

Introduction: Upadacitinib (UPA) is an oral selective and reversible Janus kinase inhibitor. UPA 45 mg once daily (QD) has demonstrated superior efficacy to placebo and a favorable safety profile following an 8-week induction therapy in patients with moderately to severely active ulcerative colitis (UC) in two double-blinded, randomized induction trials U ACHIEVE Induction (NCT02819635) and U ACCOMPLISH (NCT03653026).
Aim: This analysis evaluated the efficacy and safety of UPA following extended induction treatment (UPA 45 mg QD for 16 weeks) and subsequent maintenance treatment (UPA 15 mg QD or UPA 30 mg QD for 52 weeks).
Methods: Patients who did not achieve a clinical response (Adapted Mayo score decrease of ≥2 points and ≥30% from baseline, plus a ≥1 point decrease in rectal bleeding score [RBS] or absolute RBS ≤1) following an initial 8 weeks' UPA 45 mg QD treatment in the induction trials were eligible to receive an additional 8 week, open-label extended treatment with UPA 45 mg QD. Patients with a clinical response following completion of the extended induction (Week 16) were re-randomized 1:1 to UPA 15 mg QD or UPA 30 mg QD in the U ACHIEVE Maintenance trial (NCT02819635).
Results: Of the patients who received UPA 45 mg QD in the induction trials, 125 did not achieve a clinical response at 8 weeks and received a further 8 weeks' induction treatment. At Week 16, 73/125 (58.4%) subsequently responded and were re randomized to maintenance UPA 15 mg QD or UPA 30 mg QD. Among 16-week responders who entered the maintenance trial, a greater proportion of patients who received UPA 30 mg QD vs UPA 15 mg QD achieved the primary endpoint of clinical remission at 52 weeks (43.6% vs 26.5%, respectively), and the secondary endpoints of clinical response (78.1% vs 49.1%, respectively) and endoscopic improvement (51.3% vs 34.3%, respectively) at 52 weeks. A similar pattern was seen across all clinical, endoscopic, and histologic endpoints. At Week 52, the proportions of patients with serious adverse events (AEs) were 2.9% with UPA 15 mg QD and 10.0% with UPA 30 mg QD. Selected AEs of special interest with UPA 15 mg QD and UPA 30 mg QD included serious infection (2.9% vs 5.0% of patients, respectively), herpes zoster (0% vs 5.0%, respectively), adjudicated major adverse cardiovascular events (0% vs 2.5%, respectively), and non-melanoma skin cancer (NMSC; 0% vs 2.5%, respectively). No adjudicated venous thromboembolic events or cases of malignancy excluding NMSC were reported with either UPA dose.

Conclusions: Extended induction treatment for an additional 8 weeks with UPA 45 mg QD induced a response in over half of patients with UC who did not achieve a response after 8 weeks. The benefit of maintenance therapy in delayed responders was demonstrated with both UPA doses, although UPA 30 mg QD provided a greater benefit than UPA 15 mg QD. UPA was well tolerated with no new safety signals and selected AEs of special interest were reported infrequently with both maintenance doses.

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PATIENT PERCEPTION AND ADOPTION OF E-HEALTH MONITORING APPLICATIONS IN IBD. N. Lembrechts (1), E. Hoefkens (1), G. Dewulf (2), I. Maes (2), L. Pouillon (1), P. Bossuyt (3) / [1] Imelda Hospital, Bonheiden, Belgium, Department of Gastroenterology, [2] Inovigate, Wilrijk, Belgium, Inovigate, [3] Imelda Hospital, Bonheiden, Belgium, Department of Gastroenterology.

Introduction: E-Health applications for the management and follow-up of patient with IBD are progressively introduced in daily clinical practice. Multiple advantages are suggested for these eHealth tools, however the adoption and acceptance of these applications by the patient are understudied.
Aim: The aim was to explore digital literacy and adoption of e-Health monitoring applications in patients with IBD.
Methods: Patients attending the out-patient IBD clinic were invited to complete a questionnaire regarding the use of eHealth tools and their digital literacy.
Results: Seventy-two patients participated in the questionnaire between March 25th and June 15th 2022. The impact of the disease on their quality of life was important (VAS >4/10) in 40% of the patients. Personal perceived treatment compliance was excellent in 77% of the patients. All patients used digital communication tools on a daily basis (PC 87%, smartphone 89%, tablet 31%). One third of the patients had experience with digital medical applications. Digital tools were mainly (81%) used for medical information search on their disease and 64% of the patients communicated digitally with the health care professional. Only a minority seeks contact with other patients (10%) or made a personal follow-up report (27%). A minority of patients (22%) was reluctant against the use of smartphone based digital monitoring tools. These patients mainly feared privacy issues and an additional burden on their daily live. In contrast, patients that were open to digital monitoring tools saw mainly the tight control of the disease and the early detection of flares and side effects as potential advantages. A frequency of pushed questionnaires once a week was acceptable for patients (58%). The majority of patients was open for automated monitoring via wearables (92%) and were open to share their monitoring data in an anonymous way for research purpose (90%).
Conclusions: Patients with IBD have high digital literacy and are open to use eHealth tools in the monitoring of their disease. To reduce monitoring burden, weekly questionnaires combined with automated wearable monitoring deems most acceptable.

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SAFETY OF VEDOLIZUMAB, USTEKINUMAB AND TNF-INHIBITORS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A RETROSPECTIVE COHORT STUDY. L. Deroo (1), M. Truyens (2), J. Geldof (1), S. Akhayad (1), G. Dewitte (1), E. Glorieus (2), T. Lobatón (2) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Department of Gastroenterology and Hepatology, [2] University Hospital Ghent (UZ Gent), Gent, Belgium, Department of Gastroenterology and Hepatology; IBD research unit - Gastroenterology, Department of Internal Medicine and Paediatrics.

Introduction: The recent years, the therapeutic armamentarium for inflammatory bowel diseases (IBD) has expanded with new therapies such as the anti-alpha4beta7 integrin vedolizumab (VDZ) and anti-IL-12/IL-23p40 antibody ustekinumab (UST). However, head-to-head trials considering the safety of these newer biologics compared to tumor necrosis factor alpha inhibitors (anti-TNF) is limited. In particular, data on the safety of sequencing these biologics remains scarce.
Aim: To assess the impact of the different biologicals and previous treatments on the incidence of severe adverse events (SAE) in a real world setting of IBD patients.
Methods: A retrospective monocentric study was performed on patients with IBD under treatment with anti-TNF, VDZ or UST at the Ghent University Hospital, from January 2018 to June 2021 with follow-up until present. SAE were defined as intestinal resection, IBD disease activity-related hospitalization, hospitalization for indications related to the biologic treatment (e.g. infectious complications), malignancy and death. For the assessment of risk factors for SAE development a cox regression model was applied.
Results: A total of 267 patients were included: 84 patients started treatment with VDZ, 69 with UST, 60 with infliximab (IFX) and 54 with adalimumab (ADM). Among baseline characteristics of these treatment groups, a significant difference was found for age (younger age for IFX and ADM (P =0.001)), IBD type (percentage of patients with Crohn's disease (CD): VDZ 51.2%, UST 73.9%, IFX 70% and ADM 77.8%, P=0.003)), baseline CRP (median CRP 5 [IQR 1.6-12.4], 8.9 [2.8-19.4], 13 [1.9-31.8] and 3.2 [1-8.1] respectively for VDZ, UST, IFX and ADM, P<0.001) and baseline calprotectine (median 579 [IQR 175-1801], 752 [239-2944], 652 [65-2449] and 200 [43.7-789] for VDZ, UST, IFX and

ADM respectively, P=0.018)). Furthermore, the rate of perianal CD was higher in anti-TNF and UST groups (P=0.001) and disease duration differed significantly (9, 10, 2 and 3.5 years for VDZ, UST, IFX and ADM respectively (P<0.001)). Concomitant immunomodulator use was higher in the IFX group (81.7% vs 25% for all other groups (P<0.001)) and corticosteroid use differed among the treatment groups (VDZ 78.6%, UST 66.7%, IFX 70%, ADM 55.6% (P=0.039)). The number of prior biologicals was significantly higher in the UST group compared to other treatments (P<0.001). In total, the SAE rate was not statistically significant different between the studied biologicals (P=0.097), but there was a trend toward more SAEs in the UST (24/67, 35.8%) and IFX (20/60, 33.3%) group compared to VDZ (17/84, 20.2%) and ADM group (12/54, 22.2%). After adjustment, a significant result was found for elderly age (≥60y) (HR 1.95 95%CI[1.03-3.68], P=0.04) and a trend toward higher risk for SAE with more previous biological treatment lines (1.25 [0.99-1.57], P=0.056) and systemic corticosteroid use during treatment (1.61 [0.96-2.72], P=0.073). When assessing the subtypes of SAEs separately the intestinal resection rate was highest in the UST group (VDZ 3.6% (3/84), UST 16.4% (11/67), IFX 8.3% (5/60) and ADM 5.6% (3/54) (P=0.042). After adjustment for previous biological treatment lines, the higher risk remains in the UST vs the VDZ group (HR 3.84 95%CI[1.0-14.71], P=0.049), with a statistically different result for immunomodulator use during treatment (HR 4.82 [1.7-13.4], P=0.003). Five patients developed a malignancy (two during VDZ (colorectal carcinoma and melanoma), two during IFX (CIN3 cervix and stomach adenocarcinoma) and one during ADM (basocellular skincarcinoma) and one patient died (in the VDZ group, due to progressive melanoma). There was no statistically significant difference assessing non-IBD related hospitalization, but after adjustment there was a statistically higher risk with age ≥60years (HR 5.11 [1.94-13.43], P<0.001). Specific analyses of the difference in SAE rate between patients treated only with VDZ used as first line (n=42), anti-TNF as first line (57), and patients who already had at least one line of biologicals prior to the current one (167); the total SAE rate was numerically higher in the latter group (49/160, 30.6%) vs first line VDZ (7/42, 16.7%) and first line anti-TNF (13/57, 22.8%). Differences were not statistically significant (P=0.145), probably due to the small number of patients in the subgroups. When adjusting for potential confounders again no significant differences were seen between the treatment groups.
Conclusions: In this tertiary real-world cohort of IBD patients no statistically significant difference can be found on SAE for different treatment lines (VDZ, UST, IFX and ADM). However, a trend towards a higher SAE risk is seen in patient treated with 2 or more treatment lines, probably due to a more refractory disease.

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CLINICAL AND ENDOSCOPIC IMPROVEMENTS WITH RISANKIZUMAB INDUCTION AND MAINTENANCE DOSING VERSUS PLACEBO ARE OBSERVED IRRESPECTIVE OF NUMBER OF PRIOR FAILED BIOLOGICS.
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Introduction: In phase 3 induction (ADVANCE, MOTIVATE) and maintenance (FORTIFY) studies, risankizumab (RZB), an interleukin-23 inhibitor, was well-tolerated and superior to placebo (PBO) for inducing and maintaining clinical remission and endoscopic response in patients with moderate to severe Crohn's disease (CD) who failed/were intolerant to conventional or biologic therapy1,2
Aim: This post-hoc analysis examined efficacy and safety of RZB in patients with prior failure of biologic therapy (bio-failure) according to the number of prior biologics failed.
Methods: Clinical remission, endoscopic outcomes, and deep remission were assessed for RZB versus (vs) PBO following induction and maintenance dosing based on the number of prior biologics failed (1, 2, ≥3). Pooled Induction data were reported for PBO and RZB 600 mg intravenous (IV) q4w groups at Week (Wk) 12. Data from the withdrawal (PBO SC) and RZB 360 mg subcutaneous (SC) q8w groups were reported at Wk 52 of FORTIFY. P-values [P] for pairwise treatment comparisons were provided within each bio-failure subgroup category based on the Cochran-Mantel-Haenszel test (CMH) adjusted for strata.
Results: At baseline (BL), 48%, 25%, and 27% of patients failed 1, 2, and ≥3 prior biologics, respectively. BL characteristics were generally well balanced across subgroups, although disease duration and steroid use were slightly higher in the '≥3' subgroup. Most (90%) patients who failed 1 biologic and all who failed ≥2 biologics were anti-TNF refractory. The proportion of patients with prior vedolizumab exposure across the 1, 2, ≥3 bio-failure subgroups was 6%, 27%, and 75%, respectively; prior ustekinumab exposure was 2%, 12%, and 59%, respectively. Across the bio-failure subgroups, more patients achieved the endpoints of clinical remission and endoscopic response with RZB 600 mg IV vs PBO at induction Wk 12 (P ≤0.019). Rates of endoscopic remission, ulcer-free endoscopy, and deep remission were also

higher with RZB vs PBO among the subgroups at Wk 12. In general, greater efficacy was in observed in patients failing fewer biologics. At FORTIFY Wk 52, more patients achieved endoscopic remission (P ≤0.001), ulcer-free endoscopy (P ≤0.008), and deep remission (P ≤0.012) in the RZB 360 mg SC treatment group vs withdrawal (PBO SC) across all bio-failure subgroups; rates of clinical remission were variable across subgroups. There were no differences in treatment emergent adverse events among subgroups at induction Wk 12 or maintenance Wk 52.
Conclusions: RZB was effective and well tolerated in patients with CD irrespective of number of prior biologics failed. Achievement of endoscopic outcomes with RZB at Wk 12 and Wk 52 were lower as the number of failed biologic therapies increased. The treatment difference between RZB maintenance and withdrawal (PBO SC) for achieving clinical remission increased with the number of failed prior biologics, highlighting higher PBO rates for symptomatic improvement in less refractory patients.

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NETWORK META-ANALYSIS TO EVALUATE THE COMPARATIVE EFFICACY OF INTRAVENOUS AND SUBCUTANEOUS INFLIXIMAB AND VEDOLIZUMAB IN THE MAINTENANCE TREATMENT OF ADULT PATIENTS WITH CROHN'S DISEASE AND ULCERATIVE COLITIS. P. Bossuyt (1), L. Peyrin-Biroulet (2), D. Bettenworth (3), E.V. Loftus, Jr (4), S. Anjie (5), G. D'Haens (6), M. Saruta (7), P. Arkkila (8), D. Kim (9), D. Choi (9), W. Reinisch (10) / [1] Imelda Hospital, Bonheiden, Belgium, Gastroenterology, [2] Centre Hospitalier Régional Universitaire de Nancy,, nancy, France, Gastroenterology, [3] Medical Faculty of the University of Münster, Münster, Germany, Gastroenterology, [4] Mayo Clinic College of Medicine and Science, Rochester, Minesota, United States, gastroenterology and hematology, [5] Amsterdam UMC, Amsterdam, The Netherlands, Department of Gastroenterology and Hepatology, [6] Amsterdam UMC, Amsterdam, The Netherlands, gastroenterology and hematology, [7] The Jikei University School of Medicine, Japan, Department of Gastroenterology and Hepatology, [8] Helsinki University Central Hospital and Biomedicum, Helsinki, Finland, Gastroenterology, [9] Celltrion Healthcare, Zaventem, Belgium, NA, [10] Medical University of Vienna, Austria, Department of internal medicine III.

Introduction: Network meta-analysis (NMA) using randomised controlled trial (RCT) data can provide indirect evidence on comparative efficacy of various treatments.1 The NMA reported herein was conducted to evaluate infliximab (IFX) and vedolizumab (VDZ) comparative efficacy during maintenance treatment of moderate-to-severe Crohn's disease (CD) and ulcerative colitis (UC), covering various dosing regimens and administration routes for each biologic.
Aim: The NMA reported herein was conducted to evaluate infliximab (IFX) and vedolizumab (VDZ) comparative efficacy during maintenance treatment of moderate-to-severe Crohn's disease (CD) and ulcerative colitis (UC), covering various dosing regimens and administration routes for each biologic.
Methods: Studies were identified by literature searches that included publications up to 1 November 2022. Parallel-group RCTs evaluating IFX or VDZ (intravenous [IV] or subcutaneous [SC]) for maintenance treatment of adult patients with moderate-to-severe CD or UC that reported clinical remission rates were included. Eligible studies treated patients for a minimum of 22 weeks, with follow-up of 30–60 weeks for maintenance. Clinical remission rates in tumour necrosis factor inhibitor (TNFi)-naïve patients from each study were analysed in a Bayesian NMA fixed-effect model.
Results: Overall, 13 RCTs were identified and included in the analysis. The difference in study design between IFX (treat-through) and VDZ (re-randomisation of induction responders only) was noted. A connected network of evidence could be generated using CD and UC studies (Figures 1A and 1B, respectively). In both CD and UC, IFX SC 120 mg had the highest odds ratio (95% confidence interval [CI]) vs. placebo for clinical remission during the maintenance phase (CD: 5.90 [1.90–18.2]; UC: 5.45 [1.94–15.3]), albeit with the CIs overlapping with the CIs of the other tested regimens (Figures 2A and 2B). In both CD and UC, IFX SC 120 mg ranked highest for clinical remission among the biological agents, dosing regimens, and routes of administration tested.
Conclusions: In both CD and UC, IFX SC showed a favourable efficacy profile for achieving clinical remission during maintenance treatment of TNFi-naïve adult patients, when compared with the other IFX IV or VDZ IV/SC regimens tested.

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SCREENING FOR SARCOPENIA IN CROHN'S DISEASE: SHOULD IT BE A MUST? M. Ayari (1), M. Mtir (1), A. Chehaider (1), A. Imen (1), T. Jomni (1), H. Douggui (1) / [1] Internal Security Forces Hospital La Marsa, Tunis, Tunisia, Gastroenterology.

Introduction: Despite considerable therapeutic advances in the management of Crohn's disease (CD) over the past two decades, its course and complications remain unpredictable. Indeed, CD is associated with significant nutritional deficiencies and metabolic disturbances, including sarcopenia, defined as a loss of muscle strength and quantity, which represents a major health burden by reducing substantially the quality of life.
Aim: The aim of this study was to assess the prevalence and to determine the associated factors of sarcopenia during CD.

Methods: We conducted a retrospective single-center study, including patients followed for CD over a 7-year period [2014 - 2021]. Clinico-biological data, disease severity, and long-term outcomes (surgery and disease course) were collected. Measurement of the psoas muscle area has been applied to estimate lean muscle mass as a surrogate marker of sarcopenia, these measurements were performed on computed tomography (CT) by calculating the total psoas area at the third lumbar vertebra level. Then, the total psoas area index (TPAI) was calculated using the equation: TPAI (mm2/m2) = (Left Psoas Area (mm2) + Right Psoas Area (mm2)) / Height (m2). Sarcopenia was defined by a TPAI less than 385 mm2/m2 for female patients and 545 mm2/m2 for male patients.
Results: In total, 50 patients were enrolled with a mean age of 44.3 years [20-82], a median disease duration of 106 months and a sex ratio M/F of 3.16. Sarcopenia was observed in 14 patients (28%) with a mean TPAI of 612 mm2/m2 [1763 - 206]. Compared with patients without sarcopenia, sarcopenic patients are more likely to have a severe malnutrition (p=0.026), they had a significantly lower BMI (p=0.039); lower ferritin levels (p=0.026); lower haemoglobin levels (p=0.036); hyponatremia (p=0.028) and a lower creatinine level (p<0.0001). Sarcopenia was independent of disease location and extent. Regarding CD phenotype, we found that a structuring behaviour in the CD was significantly associated with the sarcopenia (p=0.046). Moderate to severe CD activity, as assessed by the Crohn's Disease Activity Index (CDAI) and the Harvey Bradshaw Index (HBI), was associated with sarcopenia with a p-value of 0.03 and 0.05 respectively for both indices. During the follow up, more patients with sarcopenia required biotherapy (p=0.01). Patients who underwent surgery was not in a higher risk of sarcopenia, however sarcopenia was identified as a predictive factor of the occurrence of postoperative complication with p-value = 0.05.
Conclusions: In our study, almost third of CD patients were sarcopenic. Our results suggest that sarcopenia was associated with the activity of the disease, structuring phenotype, increasing biological treatment need and major risk of postoperative complications. Systematic screening and treatment in this context should be recommended to improve the course of the disease. New potential therapeutic approach that can regulate the gut-muscle axis in inflammatory bowel disease should be investigated.

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ANALYSIS OF CLINICAL TRIAL SCREEN FAILURES IN IBD: REAL WORLD RESULTS FROM THE IOIBD.
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Introduction: Recruitment rates for phase 2b/3 randomized controlled trials (RCTs) in IBD have substantially dropped over time. Several discrete steps are required prior to successful patient randomization. Initially the physician must propose a trial to a potentially eligible patient during a pre-screening process (step 1). This is followed by patient's acceptance or refusal (step 2). Finally, after informed consent the patient undergoes trial screening to ensure they meet all eligibility criteria (step 3).
Aim: Evaluating each step separately, this study aims to assess reasons why IBD patients are not included in RCT and patients' outcome after screen failure (SF).
Methods: All IOIBD member physicians (n=58) were invited to participate. To assess steps 1 and 2, consecutive IBD patients in relapse for whom a treatment change was required were prospectively included over a 4-week period. Reasons that prevented the IBD physician offering a sponsored multicenter phase 2b/3 RCT (step 1) and reasons why the patient accepted or refused to participate (step 2) were assessed through a physician and a patient survey, respectively. Reasons for SF (step 3) from the last 6 months, including the 4 weeks of steps 1-2, were collected retrospectively.

Results: A total of 104 (59 male, 62 CD, mean age of 37.2 years) and 102 patients (58 male, 63 CD, mean age of 40.6 years) from 12 centers were included in steps 1-2 and 3, respectively. Among 104 patients in relapse for whom a treatment change was required, 41 (39.4%) were offered a RCT. Of the 28 who consented to RCT, 5 failed their screening (SF rate of 17.9%) and 23 were included. Main reasons that prevent IBD physicians from offering an RCT (step 1) were comorbidities (n=15), reluctance to accept risk of assignment to placebo (n=12) and physicians' preference for an alternate treatment option (n=12). After receiving information about RCT, major reasons why patients accepted or refused to participate included the trust they had in their IBD specialist and the risk of being assigned to a placebo, respectively (step 2). Analysis of 102 patients that were screened (step 3), main reasons of SF were insufficient disease activity (n=37; due to an insufficient endoscopic activity for 25 and to an insufficient clinical activity for 12), concurrent infection (n=15) and dropout (n=12). Half of SFs could have been avoided by thorough pre-screening. After SF, 51 patients were treated with commercially available therapy, 14 were rescreened for the same RCT (after resolution of the issue leading to SF), no treatment was required for 14, 10 were referred to surgery, 6 were screened for another RCT (the outcome was unknown for 7).
Conclusions: This first multicentric study reported a SF rate of 17.9%. Insufficient disease activity and the risk of assigning the patient to a placebo seem to be barriers to inclusion. Half of SFs could have been avoided by better pre-screening. Most of patients were treated with commercially available therapy after SF.

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EFFICACY AND SAFETY OF 2 YEARS OF CONTINUOUS OZANIMOD TREATMENT: INTERIM ANALYSIS OF THE TRUE NORTH OPEN-LABEL EXTENSION STUDY. S. Vermeire (1), P. Dulai (2), A. Dignass (3), E. Savarino (4), D. Hudesman (5), A. Afzali (6), V. Jairath (7), M. Osterman (8), L. Akukwe (9), A. Memaj (8), A. Petersen (8), A. Jain (10), J. Canavan (10), M. Abreu (11) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Chronic Diseases, Metabolism & Ageing, [2] Northwestern University, United States, Feinberg School of Medicine, [3] Agaplesion Markus Hospital, Goethe University, Germany, Medicine I, [4] University of Padua, Italy, Surgery, Oncology and Gastroenterology DISCOG, [5] NYU Langone Inflammatory Bowel Disease Center, United States, Inflammatory Bowel Disease Center, [6] University of Cincinnati, United States, Division of Digestive Diseases, [7] London Health Sciences Center at University Hospital, Canada, Gastroenterology, [8] Bristol Myers Squibb, United States, Global Drug Development, [9] Bristol Myers Squibb, United States, US Medical Affairs, [10] Bristol Myers Squibb, United States, Worldwide Medical Affairs, [11] The University of Miami Health System, United States, Crohn's & Colitis Center.

Introduction: The phase 3 True North (TN) study demonstrated the efficacy and safety of oral ozanimod 0.92 mg once daily (equivalent to ozanimod HCl 1 mg) in patients with moderately to severely active ulcerative colitis (UC). The ongoing TN open-label extension (OLE) study is exploring the long-term efficacy and safety of ozanimod in patients with UC.
Aim: To evaluate the efficacy and safety of ozanimod in patients who received 98 weeks of continuous ozanimod treatment in this interim analysis of the TN OLE study.
Methods: Patients included those who rolled over into the OLE study after achieving clinical response following 52 weeks of continuous treatment with ozanimod during the TN study (data cutoff: September 30, 2020). Nearly 73% of patients had completed Week 46 (Week 98 of continuous ozanimod treatment) of the OLE study. Endoscopy was performed annually throughout the OLE study and was scored by Mayo endoscopic score. Efficacy endpoints (clinical remission, clinical response, endoscopic improvement, and corticosteroid-free remission) were analysed using observed cases (OC) and nonresponder imputation (NRI). Safety data were also recorded.
Results: Of the 131 patients, 83 (63%) were in clinical remission, and 48 (37%) were in clinical response (but not clinical remission) upon entry to the OLE. Demographic and clinical characteristics at TN baseline were similar between these subgroups, except that a numerically higher proportion of patients in the clinical response subgroup had prior exposure to immunomodulators or anti-tumor necrosis factor. At Week 46 of the OLE study (98 weeks of continuous ozanimod treatment), a high proportion of the overall population (OC and NRI analysis) sustained clinical remission (67% and 44%), clinical response (97% and 64%), endoscopic improvement (74% and 58%), and corticosteroid-free remission (63% and 42%), respectively. By OLE Week 46, of the patients who entered the OLE in clinical response, 55% had achieved clinical remission, 50% had achieved corticosteroid-free remission, and 58% had achieved endoscopic improvement in the OC analysis; (NRI analysis: 32%, 29%, and 37%, respectively). Median partial Mayo score for the overall population of clinical responders was 6.0 points (interquartile range (IQR), 5–7) at TN baseline, 2.0 points (IQR, 1–2) at week 10 of the induction period, had stabilized by week 52 during the maintenance period (median, 1.0 points; IQR: 0–2), and was maintained through to Week 46 of the OLE study (median: 1.0 points; IQR: 0–2) in patients treated with continuous ozanimod. No new safety findings emerged from this extended analysis; 1 sudden death occurred during the OLE study and was adjudicated to be unrelated to ozanimod. Additional follow-up data will be presented.
Conclusions: This interim analysis of the TN OLE study found that a high proportion of patients who achieved clinical response or clinical remission after 1 year of ozanimod treatment sustained clinical response, clinical remission, corticosteroid-free remission, and endoscopic improvement after an additional ~1 year of treatment (98 weeks of

continuous ozanimod treatment). Patients in clinical response after a year of ozanimod treatment could achieve clinical remission with continued ozanimod therapy. No additional safety signals were observed.

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MATCHING-ADJUSTED INDIRECT COMPARISON OF UPADACITINIB VERSUS VEDOLIZUMAB AS INDUCTION THERAPY IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS. W. Reinisch (1), S. Vermeire (2), C. Hedin (3), D. Rubin (4), J. Panes (5), H. Deng (6), X. Si (7), L. Wegrzyn (8), J. Liu (9), D. Ilo (9), W. Zhou (10), Y. Sanchez Gonzalez (11), R. Panaccione (12) / [1] Medical University of Vienna, Austria, Gastroenterology and Hepatology, [2] University Hospitals Leuven, Belgium, Gastroenterology and Hepatology, [3] Karolinska University Hospital, Stockholm, Sweden, Gastroenterology, [4] University of Chicago, United States, Inflammatory Bowel Disease Center, [5] Hospital Clinic Barcelona, Spain, Gastroenterology, [6] University of Illinois, Champaign, United States, College of pharmacy, [7] Abbvie Inc., Chicago, United States, HEOR analytics, [8] Abbvie Inc., Chicago, United States, Epidemiology, [9] Abbvie Inc., Chicago, United States, Medical Affairs, [10] Abbvie Inc., Chicago, United States, Statistics, [11] Abbvie Inc., Chicago, United States, HEOR Strategy, [12] University of Calgary, Calgary, Canada, Inflammatory Bowel Disease Group.

Introduction: Upadacitinib (UPA) is a selective Janus kinase inhibitor approved in the US for patients (pts) with moderately to severely active ulcerative colitis (UC), with efficacy and safety studied in the phase 2b/3 U-ACHIEVE (NCT02819635) and the phase 3 U-ACCOMPLISH (NCT03653026) trials. Vedolizumab (VEDO) is a humanized α4β7 integrin monoclonal antibody approved for the treatment of pts with moderately to severely active UC, based on studies including the phase 3 GEMINI 1 trial (NCT00783718). The efficacy and safety of UPA compared with VEDO is unknown.
Aim: The aim of this study is to conduct placebo (PBO)-anchored matching-adjusted indirect comparison (MAIC) of efficacy and safety outcomes between UPA and VEDO in pts with moderately to severely active UC.
Methods: Data from the phase 3 induction studies U-ACHIEVE Induction, U ACCOMPLISH, and GEMINI 1 were used. Pts received UPA 45 mg oral, once daily for 8 weeks; VEDO 300 mg intravenous, at weeks 0 and 2; or corresponding PBO. Baseline characteristics for age, gender, duration of disease, total Mayo score, corticosteroid use, and fecal calprotectin levels from the UPA trials were weighted to match those reported for pts in GEMINI for efficacy plus previous anti-tumour necrosis factor/biologic therapy use/failure, Inflammatory Bowel Disease Questionnaire score, haemoglobin concentration, and white-cell count for safety. MAIC was performed for bio-naïve (no exposure to any biologic at baseline) and bio-failure (inadequate response, loss of response, or intolerance to biologic treatment at baseline) pts for efficacy outcomes and all pts for safety outcomes. Efficacy outcomes evaluated at Week 6 (VEDO)/Week 8 (UPA) were clinical remission per full Mayo score (FMS; FMS ≤2 with no subscore >1), clinical response per FMS (decrease from baseline in FMS ≥3 points and ≥30%, accompanied by a decrease in rectal bleeding score [RBS] of ≥1 or an absolute RBS of 0 or 1), and endoscopic improvement (endoscopic subscore 0 or 1). Safety outcomes evaluated were all adverse events (AEs), serious AEs (SAEs), and serious infections.
Results: MAIC utilized data from 833 UPA study pts and 351 VEDO study pts for efficacy; 848 and 374 pts for safety. A significantly greater proportion of pts receiving UPA vs VEDO in both bio-naïve and bio-failure groups achieved clinical remission, clinical response, and endoscopic improvement after weighting ($P < 0.05$). Rate differences between the UPA and VEDO cohorts for clinical remission, clinical response, and endoscopic improvement were 0.160, 0.173, and 0.270, respectively, for the bio-naïve group and 0.141, 0.374, and 0.191 for the bio-failed cohort. Safety outcomes, including the rates of AEs, SAEs, and serious infections, were not significantly different between the UPA and VEDO.
Conclusions: Greater clinical efficacy with comparable safety was achieved during induction treatment with UPA vs VEDO for pts with moderately to severely active UC based on MAIC, given the caveat of differences in onset of action rates and assessment times of the two drugs. Additional MAIC to assess longer-term outcomes are warranted.

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SARS-COV-2 ANTIBODY TITERS ANALYSIS IN IMMUNE MEDIATED INFLAMMATORY DISEASE PATIENTS AFTER COVID-19 VACCINATION: A MONOCENTRIC RETROSPECTIVE STUDY. J. Aoun (1), I. Delaleeuwe (1), A. Hoyois (1), S. Di Romana (2), C. Brasseur (2), V. Muls (1) / [1] CHU Saint-Pierre, Brussels, Belgium, Hepato-gastroenterology, [2] CHU Saint-Pierre, Brussels, Belgium, Rheumatology.

Introduction: Immune-mediated inflammatory diseases (IMID) including inflammatory bowel diseases (IBD) and inflammatory arthritides are commonly treated with biological therapies, in particular anti-TNF. Patients on anti-TNF have impaired protective immunity following pneumococcal, influenza and viral hepatitis. However, the serological response to COVID-19 vaccination is still being investigated. Recent studies demonstrated that serologic response is attenuated in IMID patients on immunosuppressive therapy.
Aim: In this study, the primary outcome is to describe the antibody response in IMID patients according to baseline patient characteristics, type of inflammatory disease, type of treatment and the disease activity. Secondary outcome is to compare antibody response in patients treated with anti-TNF, to that in patients treated with other biologic therapies.

Methods: This is a monocentric retrospective study, including 265 IMID patients followed at CHU Saint Pierre, Belgium, between 2021 and 2022. Respective baseline patient characteristics, vaccination status, treatment type, disease activity and SARS-CoV-2 antibody titers (IgG) after first, second and third vaccination were collected and analysed.
Results: A total of 265 patients were enrolled (mean age 47 years old, 35% males, 67% IBD patients). Of these, 217 patients (82%) completed the 2 doses of vaccination and 130 patients (49%) the 3 doses, while 40 patients (15%) remained unvaccinated. Antibody titers after 2 doses of vaccination were available for 50 patients. In this group, the median antibody titer was 93 AU/mL [26-421] after first vaccination, raised up to 640 AU/mL [271-800] after the second vaccination (Δ85%, $p<0.0001$). Similarly, a statistically significant increase was noted in the subgroup of patients with available serologic data after 3 vaccination doses (N=18). The median antibody titer after the first vaccination in anti-TNF subgroup (N=15) was lower than that in other biotherapies subgroup (N=23); 34 AU/mL [6-145] versus 131 AU/mL [34-704] respectively. However, after the second vaccination, higher antibody titers were found in the anti-TNF subgroup, 686 AU/mL [321-800] versus 400 AU/mL [250-800] ($p<0.388$).
Conclusions: In our cohort of IMID patients, followed at CHU Saint Pierre, Belgium, there was a statistically significant raise in antibody titers after the second and third dose of COVID-19 vaccination, regardless of the type of inflammatory disease, the disease activity, the type of treatment, and the vaccine type. Antibody titers in this particular immunocompromised population were comparable to those found in the literature for the general population. More prospective observational studies are needed with a larger sample size to determine the particular characteristics of patients with sub-optimal serological response.

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VARIABILITY IN HISTOLOGICAL ACTIVITY OF PAIRED BIOPSIES IN CROHN'S DISEASE DICTATES MULTIPLE BIOPSIES NEEDED TO ACCURATELY EVALUATE HISTOLOGICAL STATUS. M. Lenfant (1), S. Vermeire (1), J. Sabino (1), B. Verstockt (1), M. Ferrante (1), G. De Hertogh (2) / [1] University Hospitals Leuven, Belgium, Gastroenterology and Hepatology, [2] University Hospitals Leuven, Belgium, Pathology.

Introduction: At present, the significance of histologic remission in Crohn's disease [CD] is unclear. One of the main reasons is the heterogeneous distribution of the lesions. This contrasts with ulcerative colitis, where the distribution of histologic disease activity within a segment follows a homogeneous pattern and histologic scoring systems have been applied with success on limited numbers of biopsies.
Aim: We assessed the variability of microscopic disease activity in paired same-segment biopsies from CD patients.
Methods: All CD patients undergoing ileocolonoscopy between January 2020 and July 2022 at our tertiary referral center were eligible for inclusion. Clinical data were retrospectively collected from medical records. Endoscopies were video-recorded and the Simple Endoscopic Score for Crohn's Disease [SES-CD] was used to evaluate endoscopic activity. Paired biopsies were taken within the most affected area per segment, in accordance with ECCO consensus guidelines. The Global Histology Activity Score [GHAS], the Geboes Score [GS], the Robart's Histopathology Index [RHI], and the Nancy Histological Index [NHI] were determined for each biopsy by an experienced IBD pathologist [GDH] blinded to the endoscopic scores. The cut-off values for histologic remission were set at GHAS ≤ 4, GS <2B.1, RHI ≤ 3 and NI ≤ 1 [with absence of neutrophils for RHI and NI]. Variability was assessed by intraclass correlation coefficient [ICC] for continuous outcomes and by Kappa statistics for categorical outcomes. The association between histologic and endoscopic scores was studied with Spearman's rank correlation coefficient.
Results: A total of 151 biopsy pairs from 128 patients were analysed. Endoscopic activity was observed in 79% of segments. In patients with endoscopic remission [SES-CD <3], histologic disease activity [presence of neutrophils] was found in 29% of cases. There was a moderate association between the endoscopic and histological assessment, with correlation levels ranging from r 0.48 to 0.52 [$p<0.001$]. Histological activity indices showed fair agreement between paired biopsies. Looking at the predefined cut-offs, moderate variability across the different histological scores was seen. When comparing biopsies from segments with endoscopic disease activity and those without, overall higher variability in active segments and substantial agreement in paired biopsies from inactive segments [segmental SES-CD=0] was observed.
Conclusions: The patchy nature of microscopic inflammation in CD is reflected in the histological scores of paired same-segment biopsies, with only moderate agreement across histological activity indices, although lower variability was seen in biopsies from endoscopically inactive segments. Endoscopic activity only moderately reflects the histological status. Multiple biopsies per segment are therefore needed for accurate histological evaluation, the optimal number necessary remains to be explored.

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FATIGUE IMPROVEMENT CORRELATES WITH REDUCTIONS IN WORK PRODUCTIVITY IMPAIRMENT AND RELATED INDIRECT COST IN PATIENTS WITH CROHN'S DISEASE: POST HOC ANALYSIS OF PHASE 3 RISANKIZUMAB INDUCTION TRIALS. E. Louis (1), J. Panes (2), S. Ghosh (3), B. Siegmund (4), W. Lee (5), H. Deng (5), K. Kligys (5), J. Kalabic (6), E.V. Loftus, Jr. (7) / [1] CHU de Liège, Liège, Belgium, Department of

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Introduction: Patients with Crohn's disease (CD) frequently experience fatigue,1 which may reduce quality of life and work productivity, thereby contributing to patient and societal costs. Few studies have analysed the indirect cost burden associated with fatigue; this analysis used Phase 3 clinical trial data in patients with CD to assess this relationship.
Aim: This post-hoc analysis examined improvements in the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) and Work Productivity and Activity Index (WPAI) with RZB induction dosing and the indirect cost burden associated with fatigue.
Methods: The study used pooled 12-week data from patients with moderate to severe CD who received risankizumab (600 mg or 1200 mg IV) or placebo in ADVANCE and MOTIVATE. Patients completed Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) and Work Productivity and Activity Index (WPAI) questionnaires at Baseline and Week 12. All risankizumab or placebo IV treated patients with non-missing values were analysed. Correlation between FACIT-F and WPAI was assessed by Pearson correlation. Mean change from Baseline to Week 12 in WPAI was assessed and stratified by quartiles of the mean change from Baseline FACIT-F scores. The linear relationship between improvements from baseline in FACIT-F and WPAI Overall Work Impairment (OWI) was assessed; results from the regression analyses were used to calculate cost savings based on corresponding WPAI scores and average hourly wages in the US and Europe. Annualized cost savings were determined in patients who achieved a clinically meaningful improvement (≥9-unit increase) in FACIT-F and compared between patients who achieved or did not achieve a FACIT-F score > normative value (>40) at Week 12.
Results: Mean age (standard deviation) of patients was 38.4 (13.3) years and 53.1 percent were male in the study population. Moderate correlation was observed between FACIT-F and all four domains of WPAI (Pearson coefficient range ¬-0.55 to -0.30, P<0.0001) at Week 12. Greater improvements in WPAI scores from Baseline were consistently observed among patients with greater mean change from Baseline scores in FACIT-F at Week 12. A ≥9-unit change from Baseline in FACIT-F at Week 12 corresponded to a 12% reduction in OWI, which resulted in 4.8 hours of improved work productivity per week and an annualized cost savings per person of $7,749 in US and €7,117 in Europe. Patients with a normative FACIT-F score of >40 at Week 12 had a corresponding reduction in OWI score of 29%, resulting in 12 hours less work impairment per week and an annualized cost savings per person of $18,726 in US and €17,199 in Europe.
Conclusions: A significant correlation was observed between fatigue and work productivity in the induction trials of risankizumab. Early clinically meaningful improvements, as well as achieving fatigue normality, were associated with improvements in work productivity that lead to substantial indirect cost savings.

INDUCTION AND MAINTENANCE TREATMENT WITH RISANKIZUMAB LEADS TO SYMPTOMATIC RELIEF IN PATIENTS WITH MODERATE TO SEVERE CROHN'S DISEASE. E. Louis (1), J. Torres (2), J. Lindsay (3), S. Schreiber (4), R. Ungaro (5), L. Jonaitis (6), K. Kligys (7), S. van Haaren (7), E. Neimark (7), J. Zambrano (7), Y. Zhang (7), G. D'Haens (8) / [1] CHU de Liège, Liège, Belgium, Department of Gastroenterology, [2] Hospital Beatriz Ângelo, Loures, Portugal, Division of Gastroenterology, [3] The Royal London Hospital, Barts Health NHS Trust, United Kingdom, Department of Gastroenterology, [4] University Hospital Schleswig-Holstein, Germany, Department of Medicine, [5] Icahn School of Medicine, Mount Sinai, United States, The Henry D. Janowitz Division of Gastroenterology, [6] Lithuanian University of Health Sciences, Kaunas, Lithuania, Department of Gastroenterology, [7] Abbvie Inc., Chicago, United States, Medical Affairs, [8] Amsterdam University Medical Centers, Amsterdam, The Netherlands, Department of Gastroenterology.

Introduction: STRIDE II guidelines identify symptom relief as important short and intermediate treatment goals. The most burdensome symptoms reported by patients with Crohn's disease (CD) are abdominal pain (AP) and increased stool frequency (SF). Risankizumab (RZB) was shown to be well-tolerated and superior to placebo (PBO) for inducing and maintaining clinical remission and endoscopic response in patients with moderate-to-severe CD.1,2
Aim: This post-hoc analysis examined improvements in the patient reported outcomes (PROs) of AP score (APS) and SF with RZB induction and maintenance dosing and their correlation with endoscopic outcomes.
Methods: PROs using pooled data from the ADVANCE/MOTIVATE induction studies1 for the PBO and RZB 600 mg intravenous (IV) treatment groups, and data from the RZB withdrawal (PBO subcutaneous [SC]) and 360 mg RZB SC treatment groups from the FORTIFY maintenance study2, were examined. AP and number of liquid or very soft stools were recorded in a daily diary; AP was rated as none (=0), mild (=1), moderate (=2), or severe (=3). AP remission (AP ≤1) and SF remission (SF ≤2.8) were assessed. Tetrachoric correlations, used to assess the statistical correlation between two dichotomous variables, were applied to measure the association between PROs and achievement of endoscopic remission and ulcer-free endoscopy at Weeks 12 and 52.

Results: Significantly more patients receiving 600 mg RZB IV versus PBO reported improvements from baseline (BL) in SF and APS at Weeks 4, 8, and 12 (p-values <0.001). Of patients reporting AP ≥1 at Induction BL, significantly more patients receiving RZB treatment achieved APS =0 at Weeks 8 and 12 compared to PBO (p-values [p] ≤0.001). Similarly, of patients reporting SF >2.8 at BL, significantly more patients receiving RZB treatment achieved SF ≤1 at Weeks 4, 8 and 12 compared to PBO (p-values ≤0.004). At Week 52 of maintenance, more patients achieved AP remission (p <0.05) and SF remission (p <0.01) with RZB 360 mg SC compared to RZB withdrawal (PBO SC). More patients also achieved complete resolution of symptoms (APS =0 [p =0.05], or SF ≤1 [p =0.006], or AP =0 and SF ≤1 [p =0.02]). AP remission at Week 12 was weakly correlated with endoscopic remission (r=0.19; p <0.001) and ulcer-free endoscopy (r=0.17; p =0.001) at Week 12. Similarly, weak/moderate correlations of SF remission with these endoscopic outcomes were observed at Week 12 (r=0.34 [p <0.001] and r=0.35 [p <0.001], respectively). At Week 52, moderate correlations were observed with endoscopic remission or ulcer-free endoscopy and AP remission (r=0.55 [p <0.001] and r=0.50 [p <0.001]) or SF remission (r=0.59 [p <0.001] and 0.48 [p <0.001]).
Conclusions: CD-related PROs improved with RZB induction therapy, and RZB maintenance dosing led to AP and SF remission. Symptom improvements and endoscopic outcomes were moderately correlated, underscoring the importance of an objective measure to assess disease activity.

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CHARACTERIZATION OF PROTEIN DISULFIDE ISOMERASES IN ADULT AND PEDIATRIC CROHN'S DISEASE AND ASSOCIATION WITH INFLAMMATION AND FIBROSIS. E. Bequet (1), C. Salée (2), N. Blétard (3), S. Vieujean (4), C. Massot (2), F. Fonzé (2), H. Sarter (5), D. Ley (6), S. Colinet (7), P. Delvenne (3), M. Seghaye (8), E. Louis (4), M. Meuwis (2) / [1] CHU of Liège, Belgium, Paediatrics and Translational Gastroenterology Laboratory, Giga Institute, [2] CHU of Liège, Belgium, Translational Gastroenterology Laboratory, Giga Institute, [3] CHU of Liège, Belgium, Pathologic Anatomy and Cytology Laboratory, [4] CHU of Liège, Belgium, Hepato-Gastroenterology and Digestive Oncology Department, [5] Univ. Lille, Inserm, CHU Lille, Institut Pasteur de Lille, Lille, France, Institute for Translational Research in Inflammation Infinite, [6] Univ. Lille, Inserm, CHU Lille, Institut Pasteur de Lille, Lille, France, Paediatric Gastroenterology, [7] Clinique MontLégia - CHC Groupe Santé, Liège, Belgium, Pediatrics, [8] CHU of Liège, Belgium, Paediatrics.

Introduction: Evolution of Crohn's Disease (CD) is often marked by fibrostenotic complication, both in adults and in paediatrics. Although available biotherapies allow a better control of intestinal inflammation, none of them allows to prevent or treat intestinal fibrosis and surgery is often necessary, with a high risk of relapse and recurrence of stenosis. The pathophysiological mechanisms of intestinal fibrosis are multiple and poorly understood. The intestinal epithelium probably plays a key role. The endoplasmic reticulum stress (ERS) is involved in the pathophysiology of IBD and in fibrosis. Protein disulfide isomerases (PDIs) take part in the ER stress response, but their precise roles and associations with CD remain poorly characterized.
Aim: The aim of this study was to characterize within the intestinal epithelium, the distribution of specific PDIs selected previously by proteomics on CD patient's tissues with or without fibrosis, and to investigate their potential associations with inflammation, fibrosis and patient clinical parameters as age of disease onset.
Methods: Clinical data of patients from 4 tertiary hospitals were reviewed retrospectively to include tissues from 72 paediatric and 47 adult CDs, and 26 paediatric and 48 adult patients without IBD. These tissues came from intestinal resections or endoluminal biopsies. The degree of fibrosis and inflammatory infiltrate were scored by a trained pathologist. The distribution of 4 PDIs (AGR2, BiP, PDIA6 and ERP44) was studied on immunohistochemistry (IHC) treated tissues and scored using a semiquantitative scale (0 to 4). Statistical tests as ANOVA or Kruskal-Wallis (with post hoc test), T-Student and Mann-Whitney were used to assess associations of IHC score within the epithelium (surface, median crypts and bottom of the crypts) with inflammation, fibrosis grade, segment location and clinical parameter including age of disease onset.
Results: The CD cohort counted 72 paediatric-onset: 40 B2, 32 B1 according to the Paris classification, and 47 CDs with adulthood-onset: 28 B2, 19 B1 according to the Montreal classification. The non IBD cohort counted 26 paediatric tissues and 48 adult tissues, both from biopsies or surgical margins for an indication other than IBD. The median (range) ages at intestinal resection surgery were respectively 15.95 (7.97-36.53) and 35.71 (18.80-70.84) years. Ileo-colic stenoses were more frequent in paediatric-onset CD patients while ileal stenoses were more frequent in adulthood-onset CD, with a majority of primary stenoses in both. The PDIs showed an IHC signal which was mainly epithelial. The distribution of PDIs differed according to the segment (colon or ileum), the age of CD onset, the epithelium location (surface, median crypt, or bottom of the crypt), and the normal, inflammatory, and/or fibrotic features of the tissues. In the ileum of adult and paediatric CDs, the distribution of AGR2 was significantly higher in the epithelium adjacent to fibro-inflammatory tissues (p<0.01). In paediatric cases, AGR2 signal increased significantly together with fibrosis grades within the ileal surface epithelium (p<0.0001). The distribution of the other PDIs (BiP, ERP44, and PDIA6) was rather influenced by the inflammatory infiltrates and varied in adult and paediatric CD. The distribution of BiP was significantly higher in tissues with acute and/or chronic inflammation and independent from fibrosis grade. In adults, the distribution of PDIA6 in the colonic epithelium was significantly higher in CD cases compared to non-CD cases.

Conclusions: Our tissues PDI characterization revealed different associations with inflammation, fibrosis, tissue locations and clinical parameters which suggest that the studied PDIs may have different roles in the ERS response within the intestinal epithelium in adult and paediatric CD. However, these PDIs need to be functionally explored further to better understand their specific involvement in inflammation and fibrosis in CD. The increase of AGR2 in fibro-inflammatory tissues, not observed with other PDIs, suggests a specific link between AGR2 and intestinal fibrosis.

- I39 -

MULTI-LOCUS GENETIC RISK FOR THE EARLY DEVELOPMENT OF FIBROSTENOSIS IN PATIENTS WITH CROHN'S DISEASE. T. Holvoet (1), S. Fouquaert (2), J. Celis (3), P. Bossuyt (4), I. De Kock (5), P. Hindryckx (3), E. Louis (6), M. Georges (6), S. Vermeire (4), M. De Vos (3), I. Cleynen (7), D. Laukens (3) / [1] Vitaz, Sint-Niklaas, Belgium, Department of Gastroenterology, [2] Ghent University, Ghent, Belgium, VIB - UGent Center for Inflammation Research (IRC), [3] Ghent University, Ghent, Belgium, Ghent Gut Inflammation Group (GGIG), [4] University Hospitals Leuven, Belgium, Department of Gastroenterology and Hepatology, [5] Ghent University Hospital, Ghent, Belgium, Department of Radiology, [6] CHU Liege, Liège, Belgium, Department of Gastroenterology, [7] KU Leuven - University of Leuven, Leuven, Belgium, Department of Human Genetics.

Introduction: The number of patients suffering from inflammatory bowel diseases, including Crohn's disease (CD), has risen considerably over the past decade. Fibrostenosis is a complication of CD occurring in at least 30% of patients. Attempts to identify genetic markers for fibrostenotic CD have been hampered by poor and subjective characterization of the study population.
Aim: The aim of this study was to identify genetic markers by focusing on early, well-defined fibrostenotic CD.
Methods: In this multicenter, retrospective, nested case-control association study, early ileal fibrostenotic CD was defined based on computed tomography or magnetic resonance enterography and occurring within five years following diagnosis. (N=248) The control cohort consisted of ileal CD patients without fibrostenotic or penetrating complications for a minimum of ten years. (N=56) Associations were evaluated using Immunochip and positive associations were assessed in a replication cohort (N(cases) = 46, N(controls) = 71) by Taqman assays.
Results: Based on logistic regression, we discovered five SNPs in the discovery cohort with P-values < 10^-4. The association of one SNP (rs17106237) was validated in the replication cohort with a P-value < 0,05. Based on eleven associated SNPs, we calculated a genetic risk score (GRS) for each patient. Using a cut-off based on the area under the curve (0,925), patients from the replication cohort were assigned to a low or high GRS group. Interestingly, the time to development of fibrostenosis was linked with the GRS (Mantel-Cox test: P = 0,138); 26% of patients in the low GRS group were diagnosed with fibrostenosis four years after diagnosis compared to 42% in the high GRS group. This observation is however not significant since it is currently underpowered and will require the inclusion of additional patients.
Conclusions: This carefully phenotyped association study reveals a genetic contribution to the early development of fibrostenosis in ileal CD.

- I40 -

GENERAL DECREASE IN BACTEROIDES-2 ENTEROTYPE AFTER FMT IN UC AND BASELINE RNA AND MICROBIOTA SIGNATURES ARE ASSOCIATED WITH RESPONSE. S. Deleu (1), C. Caenepeel (1), S. Verstockt (1), J. Vazquez Castellanos (2), K. Arnauts (1), S. Braeckeleire (1), K. Machiels (1), F. Baert (3), L. Pouillon (2), P. Hindryckx (4), T. Lobatón (4), E. Louis (5), D. Franchimont (6), B. Verstockt (7), M. Ferrante (7), J. Sabino (7), S. Vieira-Silva (8), G. Falony (2), J. Raes (2), S. Vermeire (7) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing, [2] KUL - University of Leuven, Leuven, Belgium, Department of Microbiology and Immunology, [3] AZ Delta, Roeselare, Belgium, Department of Hepatology and Gastroenterology, [4] University Hospital of Ghent, Belgium, Department of Hepatology and Gastroenterology, [5] CHU Liege, Liège, Belgium, Department of Hepatology and Gastroenterology, [6] Erasme Hospital, Brussels, Belgium, Department of Hepatology and Gastroenterology, [7] University Hospitals Leuven, Belgium, Department of Hepatology and Gastroenterology, [8] University Medical Center of the Johannes Gutenberg-University Mainz, Germany, Institute of Medical Microbiology and Hygiene and Research Center for Immunotherapy.

Introduction: The efficacy of faecal microbiota transplantation (FMT) in UC has been reported to be donor-, patient- and procedure-dependent (Rees et al., 2022). The RESTORE-UC trial [NCT03110289] aimed to improve the outcome of FMT in patients with active UC by donor preselection on microbiota level, a strict anaerobic preparation and repeated FMT administration. The trial was prematurely stopped for futility (Caenepeel et al., 2022).
Aim: We investigated changes in resp. biopsy and faecal samples obtained host transcriptomics and microbiota profiles from baseline to primary endpoint (PE) at week 8 to understand reasons for the observed lack of efficacy.
Methods: Active UC patients (total Mayo score 4-10 with endoscopic sub-score >=2, n=72) were randomly allocated to receive 4 anaerobic-prepared superdonor (S) FMT or autologous (A) FMT. Primary endpoint was defined as steroid-

free clinical remission (Total Mayo ≤ 2, with no sub-score >1). Host RNA extractions were performed from mucosal biopsies collected at week 0 (n=63) and 8 (n=54) using the Qiagen AllPrep DNA/RNA Mini kit, and sequenced using Illumina HiSeq4000. Sequencing data was further processed (read-count filtering, normalization) and further analyzed using DESeq2 package. Corresponding faecal samples (resp. n=62 and n=50) were submitted to DNA extractions using MagAttract PowerMicrobiome DNA/RNA kit on an automated extraction platform, followed by library prep and 16S rDNA-sequencing using Illumina MiSeq. The obtained sequences were subjected to the DADA2 pipeline in R and the Quantitative Microbial Composition (QMP) was quantified by flow cytometry.
Results: Eight responders were observed: 3 after S-FMT and 5 after A-FMT, as well as 58 non-responders considering the intention-to-treat population. Responders to FMT tended to cluster at baseline (adonis p=0.34) and PCA analysis on the top 500 mucosal genes with the highest variance, showed a significant host effect at week 8 between responders and non-responders (adonis p<0.05). Likewise, PCA analysis of the currently available QMP showed a trend towards clustering by response at week 0 and 8 resp. adonis p=0.18 and p=0.11). An overall decrease in Bacteroides-2 enterotype prevalence was observed over both treatment groups and independently from reaching the PE (All McNemar's p=0.077).
Conclusions: A trend towards clustering of responders on host mRNA level and QMP was observed at baseline as well as at the primary endpoint, showing a potential role for pre-FMT patient selection by phenotype. Moreover, the dysbiotic enterotype Bacteroides-2 seems to be decreased after FMT. However, further analyses are mandatory to identify specific predictors of response and the origin of the microbiota shift.

- I41 -

IBD PATIENTS WITH POSITIVE ANTI-NUCLEOCAPSID SEROLOGY (OR HISTORY OF COVID-19 INFECTION) HAVE HIGHER ANTI -SARS- COV2 SPIKE-SPECIFIC IGG ANTIBODY LEVELS FOLLOWING 2-AND 3-DOSE SERIES VACCINATION. A. Hoyois (1), C. Gulkilik (1), L. Mekkaoui (2), H. Dahma (2), V. Wambacq (1), C. Minsart (1), N. Rosewick (3), E. Quertinmont (3), A. Van Gossum (1), C. Liefferinckx (1), L. Amininejad (1), A. Cremer (1), O. Vandenberg (4), D. Franchimont (1) / [1] HUB Hôpital Erasme Brussels, Brussels, Belgium, Department of Gastroenterology, Hepatopancreatology, and Digestive Oncology, [2] LHUB-ULB Laboratoire Hospitalier Universitaire de Bruxelles, Brussels, Belgium, Microbiology Department, [3] HUB Hôpital Erasme Brussels, Brussels, Belgium, Laboratory of Experimental Gastroenterology, [4] LHUB-ULB Laboratoire Hospitalier Universitaire de Bruxelles, Brussels, Belgium, Innovation and Business Development Unit.

Introduction: COVID-19 vaccine-induced antibody response is attenuated in Inflammatory Bowel Disease (IBD) patients taking Infliximab, Infliximab plus Thiopurine or Tofacitinib. Very few studies described the impact of COVID-19 infection on the 2-dose series and booster vaccine response in IBD patients.
Aim: The aim of this prospective cohort study is to assess anti-SARS-CoV2 spike-specific IgG antibody levels in IBD patients over one-year follow-up and whether previous history of COVID-19 infection, anti-nucleocapsid serology and immunosuppressive treatments were associated with different anti-SARS-CoV2 antibody 'response after 2-dose series and booster vaccine.
Methods: This is a prospective, single-centre study, conducted in HUB - Erasme Hospital (ULB) between January 2021 and May 2022. Three questionnaires were completed at 6-months intervals. Data collected include IBD demographics and phenotyping, immunosuppressive treatments, vaccination and history of COVID-19 infection. Anti- SARS-CoV2 spike-specific IgG and anti-nucleocapsid antibody measurements were made before COVID-19 vaccine (T1), after 2-dose (T2) and after booster' vaccine (3- or 4- dose, T3). To determine the impact of immunosuppressive treatments on antibody levels, each treatment group was compared with non-immunocompromised group as defined by "no treatment or 5-aminosalicylic acid ». Approved by Erasme EC (CCB B4062020000091)
Results: From a pre- listing of 2349 IBD patients, 492 IBD patients were enrolled. Of these, 234 patients completed their follow-up. Seroprevalence for anti-SARS-CoV2 spike-specific IgG of COVID-19 infection was 17,1% before vaccination. 92,3% (216/234) patients received the initial vaccination 2-dose series and 87,5% (189/216) patients received one or two booster vaccine doses. Median anti-SARS-CoV2 spike-specific IgG titres significantly increased after 2-dose series and after booster vaccine (698,5 BAU/mL (IQR, 190,3 – 1515) and 2480 BAU/mL (IQR, 1590 – 6820) respectively (p < 0,0001)). Positive anti-nucleocapsid serology (or history of COVID-19 infection) significantly increased median anti-SARS-CoV2 spike-specific IgG titres after 2-dose series vaccine (1930 BAU/mL (IQR, 756,5 - 3483) versus 521 BAU/mL (IQR, 146,5 - 1048) p < 0,0001) and after booster vaccine (4390 BAU/mL (IQR, 1730-9900) versus 2160 BAU/mL (IQR, 1500 - 5600) p=0,0156). Interestingly, Immunosuppressive treatments did not reduce antibody levels in patients with history of COVID-19 infection or positive anti-nucleocapsid serology. After 2-dose series vaccine, median anti-SARS-CoV2 spike-specific IgG titres was 2150 BAU/mL (IQR, 771,5 – 3575) in non-immunocompromised patients (n=18) and 1780 BAU/mL (IQR, 717,8 – 2630) in immunocompromised patients (n=22) (p = 0,352). After booster vaccine, median anti-SARS-CoV2 spike-specific IgG titres was 4230 BAU/mL (IQR, 1548 – 9910) in non-immunocompromised patients (n=20) and 4225 BAU/mL (IQR, 1823 – 9070) in immunocompromised patients (n=36) (p = 0,976). In our multivariate models, lower antibody concentrations were independently associated with anti-TNF (0,57 (95% CI 0,45 – 0,71) p < 0,0001) in T2 and associated with anti-TNF (0,77 (95% CI 0,64 -0,93) p = 0,0064) and anti-TNF plus thiopurine (0,51 (95% CI 0,37 – 0,71) p = 0,00013) in T3. Higher antibody concentrations

were independently associated with anti-nucleocapsid antibody positiveness (2,23 (95% CI 1,55 – 3,19) p < 0,0001) and mRNA vaccine (2,22 (95% CI 1,81 - 2,72) p < 0,0001) in T2 and associated with anti-nucleocapsid antibody positiveness (1,72 (95% CI 1,32 – 2,26) p = 0,00011) in T3.
Conclusions: IBD patients with positive anti-nucleocapsid serology (or history of COVID-19 infection) have higher anti-SARS-CoV2 spike-specific IgG antibody levels following 2-and 3-dose series vaccination. Anti-SARS-CoV2 spike-specific IgG antibody levels are reduced in patients taking anti-TNF and anti-TNF plus thiopurine after 2-dose series vaccine and booster vaccine, respectively. However, in most immunosuppressive treatments, anti-SARS-CoV2 spike-specific IgG antibody levels are significantly higher following booster vaccine than following 2-dose series vaccine. Booster vaccine should be continued in patients on immunosuppressive treatments, particularly those on anti-TNF therapy.

- I42 -

FIBROSTRICTURING CROHN'S DISEASE IS CHARACTERISED BY AN IMBALANCE IN ACTIVE EOSINOPHILS, TH1, TH2 AND REGULATORY T CELLS. I. Jacobs (1), B. Ke (2), J. Cremer (2), A. D'hoore (3), G. Bislenghi (3), G. Matteoli (2), G. De Hertogh (4), J. Sabino (2), M. Ferrante (2), S. Vermeire (2), C. Breynaert (5), T. Vanuytsel (2), B. Verstockt (2) / [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, [3] University Hospitals Leuven, Belgium, Department of Gastroenterology and Hepatology, [4] KUL - University of Leuven, Leuven, Belgium, Department of Imaging and Pathology, [5] KUL - University of Leuven, Leuven, Belgium, Department of Microbiology, Immunology and Transplantation.

Introduction: About one third of patients with Crohn's disease (CD) develop strictures during their disease course requiring surgical resection. The immune landscape involved in this process is poorly understood.
Aim: Therefore, we aimed to characterise the fibroblast phenotype, immune cells and their mediators involved in intestinal strictures.
Methods: We included 25 CD patients with stricturing disease in the terminal ileum (TI) and 10 controls with colorectal cancer (CRC), all undergoing an ileocolonic resection. Transmural samples from the resection specimen of the TI were obtained. Macroscopically, CD tissue was divided into unaffected, fibrostenotic and inflamed regions by an experienced histopathologist. Next, mucosa was separated from deeper layers, after which single cells were isolated and fluorescently stained for flow cytometry. Protein levels were determined via the MesoScale Discovery (MSD) platform in the corresponding samples. Comparisons between CRC controls and CD patients were performed via an unpaired t-test or Mann-Whitney analysis and corrected for multiple testing.
Results: An increase in active fibroblasts and decrease in inactive fibroblasts in the fibrotic and inflamed mucosa ($p=0.0002$ and $p<0.0001$) and deeper layers ($p=0.003$ and $p=0.02$) when compared to the CRC controls was observed, confirming ongoing tissue remodelling. An enrichment of active eosinophils was only seen in the fibrotic deeper layers ($p=0.02$), although an increase in T helper 2 (Th2) cells was observed in both the fibrotic and inflamed deeper layers ($p=0.02$ and $p=0.04$). In contrast, T helper 1 (Th1) cells were decreased in both fibrotic and inflamed mucosa ($p=0.03$ and $p=0.02$) and deeper layers ($p=0.01$ for both). Regulatory T cells were significantly enriched in both fibrotic and inflamed mucosa ($p<0.0001$ and $p=0.0005$) and deeper layers ($p=0.01$ and $p=0.006$). Protein quantification confirmed a significant increase in transforming growth factor-β3 (TGF-β3) in the fibrotic ($p=0.007$) and inflamed ($p=0.0002$) deeper layers, but not in the more superficial mucosa. Comparably, IL-1β was increased in the fibrotic ($p=0.05$) and inflamed ($p=0.05$) deeper layers. A similar observation was made for basic fibroblast growth factor (bFGF) ($p=0.004$), although only a trend could be seen in the fibrotic deeper layers ($p=0.08$).
Conclusions: The fibrotic and inflamed tissue of CD patients is characterized by increased activated eosinophils, Th2 and regulatory T cells and decreased Th1 cells, as well as many of their mediator cytokines. The current immunological characterisation can help to prioritise potential anti-fibrotic targets for stricturing CD.

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COMPARISON AND OPTIMIZATION OF CALPROTECTIN EXTRACTION METHODS IN ROUTINE IBD CARE. E. Vermeulen (1), L. Pouillon (2), B. Possemiers (1), A. Goovaerts (1), I. Geerts (1), P. Bossuyt (2) / [1] Imelda Hospital, Bonheiden, Belgium, Laboratory Medicine, [2] Imelda Hospital, Bonheiden, Belgium, Gastroenterology.

Introduction: The preanalytical phase contributes to variability in calprotectin measurements between laboratories while tight control of patients with IBD relies on accurate and precise calprotectin results. The 'weighing-based' extraction method is considered to be more accurate for calprotectin than 'volume-based' methods. However, weighing-based methods are challenging in routine practice. This procedure is labor-intensive and poses a risk for identification errors and other preanalytical concerns in a batch extraction setting - such as prolonged sample storage and freeze-thaw cycles. The consolidation of calprotectin samples from four hospitals in our laboratory network urged us to re-evaluate the preanalytical phase of calprotectin measurement.

Aim: Our aim was to optimize the preanalytical phase in calprotectin analysis, by comparison of three different calprotectin extraction methods combined with a single analytical method, the EliA™ Calprotectin 2 test (Thermo Fisher Scientific).
Methods: From February 2022 onwards, 50 prospective calprotectin samples underwent simultaneous calprotectin extraction with 3 methods. The reference method (the current extraction method in our lab), a weighing-based method (Fecal sample preparation kit®; Roche Diagnostics) was compared with two volume-based (dipstick) methods (CALiaGold® pierceTube; Sentinel diagnostics, and Elia™ Stool Extraction Kit plus; Thermo Fischer Scientific). The extracts were measured simultaneously to eliminate difference in sample or extract storage and to minimize analytical (interrun) variability.
Results: Both the volume-based extraction methods correlate well with the reference method (Pearson's R>0.98). At the diagnostic cut-off of 50 mg/kg, there is a good concordance in terms of positive or negative results, between the extraction methods. Of 26 negative (calprotectin <50 mg/kg) samples obtained with the reference method (Roche), 25/26 samples were also negative with the alternative extraction methods. The discordant samples had low positive values: 54 mg/kg for the discordant Caliagold® extract, compared to 35 mg/kg with the reference method and 42 mg/kg with Elia™ Stool Extraction Kit plus; the discordant Elia™ Stool Extraction Kit plus extract measured 72 mg/kg compared to 41 mg/kg with the reference method and 34 mg/kg with Caliagold extraction. In 24 positive samples with a calprotectin result >50 mg/kg with the reference method, the concordance for positivity is 23/24 for Elia™ Stool Extraction Kit plus and 21/24 for the Caliagold extraction. All discordances – gaining a negative result with the alternative extraction methods - were borderline results with the reference method (ranging 56-65 mg/kg). In positive samples >50 mg/kg, the Caliagold extraction gained lower results with a median negative bias of -28.4% (95%CI -45.7 to 0.0), even ranging to -74.3% (267 mg/kg compared to 1040 mg/kg with the reference method) in one sample. The Elia™ Stool Extraction Kit plus showed a median bias of 11.1% (95%CI: -24% to 40%) and less variability – especially in the clinically important range of 100-300 mg/kg, with the exception of some distinct discordant results. However, when these discordant samples were repeated with a good homogenisation of the samples before repeating both extractions, the Elia™ Stool Extraction Kit plus (Thermo Fisher Scientific) and the Fecal sample preparation kit® (Roche) gained comparable results and even confirmed the result obtained with the Elia™ Stool Extraction Kit plus.
Conclusions: The 'volume-based' (or 'dipstick') calprotectin extraction method Elia™ Stool Extraction Kit plus (Thermo Fischer Scientific) was judged clinically equivalent to the 'weighing-based' gold standard Fecal sample preparation kit® (Roche Diagnostics), while another 'volume-based' calprotectin extraction method (CALiaGold® pierceTube; Sentinel diagnostics) was not. Since the Elia™ Stool Extraction Kit plus (Thermo Fischer Scientific) can be performed daily - excluding the need to freeze samples, has a lower risk for identification errors and facilitates a good homogenization of the faecal sample, it might be the preferred technique in a large-volume clinical lab.

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

- K01 -

SEASONAL EOSINOPHILIC ESOPHAGITIS: HOW TO DIAGNOSE? J. Bosmans (1), S. Van Biervliet (1), M. Van Winckel (1), R. De Bruyne (1), P. De Bruyne (1), S. Vande Velde (2) / [1] Ghent University Hospital, Ghent, Belgium, paediatric gastroenterology, [2] Ghent University Hospital, Ghent, Belgium, Paediatric Gastroenterology.

Introduction: Guidelines on eosinophilic esophagitis (EoE) from Espghan (2014) and BSPGHAN (2022) mention seasonal distribution. But how to diagnose seasonal EoE?
Case report: A 12-year-old boy had in 2014 an endoscopic diagnosis of EoE with 100 Eosinophils per high power field (HPF). Esophageal eosinophils dropped to 25/HPF with a cow's milk free diet and secondly adding local budesonide. Thereafter, he was evaluated every 6 months using the validated PEESS (paediatric eosinophilic esophagitis symptom score), and yearly endoscopically. In 2017 he developed hay fever symptoms based on a grass pollen allergy (RAST >100 kU/L). The EoE flared clinically and endoscopically (>100 eosinophils/HPF) while still treated with diet and budesonide. During the winter, symptoms disappeared (PEESS 8/100) and the diet and budesonide were gradually downgraded and stopped. An endoscopy in January showed no eosinophils. In July 2022 the PEESS increased to 35/100 and the endoscopy revealed > 100 eosinophils/HPF. This pattern of symptoms suggested a seasonal EoE. Currently, this boy is treated with local budesonide during grass pollen season.
Conclusions: Several studies proved seasonal distribution in EoE. Ram et al. (2015) described the presence of seasonal exacerbations in 2.7% (32/1180) (1/40) of children diagnosed with EoE. These children had a concomitant diagnosis of allergic rhinitis. Seasonal EoE was diagnosed when eosinophils/HPF in the biopsy of two consecutive endoscopies performed in different seasons displayed a 2-fold increase without treatment changes. Reed et al. (2020) describe a seasonal EoE frequency of 2% (13/782) (1/50), diagnosed in the same manner as the study from Ram et al. This is comparable with the results of our center as we follow 40 children with EoE of which 1 was diagnosed with seasonal EoE. In conclusion, seasonal distribution by aero-allergens is accepted as a potential role in EoE. We present a case of seasonal EoE. Diagnosis should be made by performing an endoscopy during different aero-allergen seasons with at least a two-fold increase in eosinophils without changing treatment. The frequency of seasonal EoE is rather low (1/40 to 1/50).

- K02 -

ESOPHAGOCOLOPLASTY: NEAR 30 YEARS FOLLOW-UP FOCUSING ON QUALITY OF LIFE. G. De Peuter (1), T. Lerut (1), J. Moons (1), H. Van Veer (1), P. Nafteux (1), L. Depypere (1) / [1] KUL - University of Leuven, Leuven, Belgium, Medicine.

Introduction: A colon interposition (CI) is commonly used as an oesophageal replacement, when the stomach is not available or desirable for a gastric pull-up. Indications are mostly malignant disease, atresia, perforation or caustic burn of the oesophagus.
Aim: Since there is in literature only little information about very long-term outcome, our aim was to investigate the long-term quality of life (QoL), and more specific quality of feeding and digestion in patients with a CI.
Methods: Our patient population consisted of 190 patients, who underwent this operation between 1979 and 2006 at the same tertiary referral center. Thus, obtaining a follow-up period from at least 15 years. In 1996, a similar study was done, with partially the same patient population (CI's between 1979 and 1993). We have used the same quality of life questionnaire (QOL-Q) (dietary difficulties, gastrointestinal complaints, impact on daily life, satisfaction, etc.) in order to enable comparison. We contacted patients by phone to ask for participation, questionnaires were sent by post or email. Ethical approval was obtained.
Results: One hundred nineteen patients have died and 7 are lost to follow-up. Of 64 survivors, response rate is 87.5%, with a mean follow-up of 29.5 years. 41.1% are atresia patients, 23.2% caustic burn, 16.1% malignant and 19.6% other reasons. 82.1% has a BMI >18.5. 71.4% can eat a normal meal including bread, meat and vegetables. 30.4% still has daily swallowing difficulties. Mean satisfaction score was 8.4±0.29 (CI 95%) on 10. Same results are found when atresia patients were analyzed separately. Comparison with the previous QOL-Q's cannot detect relevant differences over time.
Conclusions: In this first single-center re-evaluation with now an average of 29.5 years follow-up, most long-term survivors have an acceptable QoL and can take nutrition well. Swallowing problems occur mainly when eating tough meat and as they adapt, it's often tolerable. Concluding, almost all respondents do have residual symptoms, but no major problems are identified. Provided some adjustments, long term quality of living and eating is certainly acceptable and sustainable.

- K03 -

EXPLORING PARENTAL THOUGHTS AND CLINICAL EXPERIENCES ON BLENDED FOOD IN A PEDIATRIC POPULATION, A QUALITATIVE STUDY. R. Verheije (1), F. Carbone (2), T. Bosmans (1), K. van Hoeve (1), I. Hoffman (1) / [1] University Hospitals Leuven, Belgium, Paediatrics, [2] University Hospitals Leuven, Belgium, Gastroenterology.

Introduction: There is an increased interest of blended food (BF) as an alternative to Commercial Food in tube fed children.
Aim: The aim of this study was to explore parental experiences and evaluate whether BF is an appropriate alternative in children, assessed by anthropometric evolution, dietary alterations, biochemical nutritional status and medication changes.
Methods: In this cross-sectional study, we included all children who were on BF at University Hospital Leuven in March 2022 and where parents were willing to complete a patients satisfaction questionnaire. Patient's charts were retrospective analysed. Parent satisfaction score was calculated by using cumulative scores on 17 questions (scale from one to five). A score of 51 points, indicating an average score of more than 3 per question, was considered significant.
Results: Nine children receiving BF were identified (median age 4.7 [2-13] years, median weight 14 [8,6 - 35,3] kg, and 66% male). All parents were satisfied using BF based on the parent satisfaction score (> 51 points). Main reason to switch to BF according to parents were less food processing discomforts. Additional results showed no clinically relevant weight changes (no drop ≥ 1 SD line in weight-for-age growth chart). No patients needed to discontinue BF, although in five patients alterations in BF were made by the dietician. Nutritional deficiencies (iron ± zinc deficiency) were present in four patients, although timing of onset of deficiency was unsure due to retrospective study design.
Conclusions: Based on parental and clinical experiences BF was well tolerated. A standard follow-up scheme is proposed, in addition to the guidance by an experienced medical team to ensure successful outcomes.

- K04 -

SELF-REPORTED PRESCRIBING BEHAVIOUR OF VITAMIN D PROHYLAXIS IN HEALTHY CHILDREN BY BELGIAN PAEDIATRICIANS. C. De Crem (1), M. Van Winckel (2), A. Raaijmakers (3), Y. Vandenplas (4), S. Van Biervliet (2) / [1] Ghent University, Ghent, Belgium, Paediatrics, [2] Ghent University Hospital, Ghent, Belgium, Paediatrics Gastroenterology, [3] ZNA Antwerpen, Antwerpen, Belgium, Paediatrics, [4] UZ Brussel, Belgium, Paediatrics Gastroenterology.

Introduction: Currently, there is no uniformity in guidelines regarding vitamin D prophylaxis in healthy children.
Aim: In this context, the practice of vitamin D prophylaxis of Belgian paediatricians was explored by a questionnaire survey.
Methods: Between June and September 2022, a questionnaire was sent by e-mail to all Belgian paediatricians that are a member of a scientific or professional organization and to the head of every Belgian paediatric hospital ward.
Results: We received 536 questionnaires, of which 407 were answered completely. All answers were included in our analysis. All regions, age categories and subspecialties were represented. Vitamin D prophylaxis was always or frequently advised by 97,6% of paediatricians. However, only 58% of paediatricians advise vitamin D prophylaxis up to the age of 6 and 66% of paediatricians advise a daily dose of 400 IU. The dosage and/or duration of Vitamin D prophylaxis is adjusted based on skin colour by 71.1 % of paediatricians. Approximately 40% of paediatricians adjust the dosage by seasonality and the amount of sun exposure. 25-OH vitamin D is frequently to always measured, in case a blood examination is indicated for other reasons, by 56% of paediatricians. In nearly every hospital (96,5%) there is a specific protocol for vitamin D prophylaxis on the maternity ward. In contrast, only 30% of all heads of service confirmed the existence of a protocol for vitamin D prophylaxis on the paediatric ward.
Conclusions: Belgian paediatricians uniformly prescribe vitamin D prophylaxis to infants. Reported practices regarding duration and dosing of vitamin D prophylaxis show large diversity. Most paediatric wards do not have a protocol. To our knowledge, this is the first study investigating the reported prescribing behaviour of vitamin D prophylaxis of Belgian paediatricians in healthy children.

- K05 -

HIGHER DRUG EXPOSURE, BUT NOT TROUGH CONCENTRATIONS OF INFLIXIMAB, CORRELATES WITH RATE OF INFLIXIMAB INDUCED SKIN LESIONS IN PAEDIATRIC IBD PATIENTS. K. van Hoeve (1), D. Thomas (2), I. Hoffman (3), E. Dreesen (2) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Paediatric gastroenterology & Hepatology & Nutrition, [2] KU Leuven - University of Leuven, Leuven, Belgium, Department of Pharmaceutical and Pharmacological Sciences, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Paediatric gastroenterology & Hepatology & Nutrition.

Introduction: Although infliximab (IFX) therapy has revolutionised treatment of inflammatory bowel disease (IBD) patients, there is still high variability in response necessitating drug optimisation. While higher IFX trough levels (TLs)

are associated with better outcomes, this could serve as a risk for more adverse events (AEs), including IFX-induced skin lesions.
Aim: Therefore, we studied the correlations of IFX exposure with the occurrence of AEs in paediatric patients with IBD.
Methods: In this single-centre study, all children with Crohn's disease (CD) and ulcerative colitis (UC) receiving maintenance IFX therapy who underwent pro-active drug monitoring between March 2015 and August 2022 were included. IFX doses/intervals and patient characteristics were prospectively registered, including appearance of AEs or skin lesions. IFX TLs were analysed using apDia IFX ELISA kit. Data are presented as median with interquartile ranges [IQR] and hazard ratio (HR) with 95 % confidence intervals [95% CI].
Results: A total of 109 patients (72 CD and 37 UC; 48% male; median age at IFX start of 12.9 [11.5-15.0] years) contributed 2913 IFX TLs (median 23.0 [11.0-39.0] per patient) at 3042 infusion visits. During a median follow-up of 3.0 [1.5-4.5] years, we observed 684 AEs in 101 patients and 49 skin lesions in 35 patients. AEs were mainly represented by upper respiratory tract infections (n=333, 48.7%), gastroenteritis (n=130, 19.0%), and pharyngitis or tonsillitis (n=84, 12.3%). Thirty-eight confirmed COVID-19 cases were reported (23 patients were fully vaccinated), all with a mild course. There was no significant difference (p=0.467) in median TLs between patients with (8.1 [5.8-9.2] µg/mL) and without (8.1 [6.2-10.0] µg/mL) skin lesions. However, Cox proportional hazard modelling showed that higher median IFX doses [HR 1.084 (1.024-1.148), p=0.005] were associated with increased risk of skin lesions, additionally to female sex [2.210 (1.187-5.310), p=0.016] and CD [1.695 (1.241-1.877), p=0.011]. Considering IFX therapeutic TL cut-offs of <5.0 and >9.0 µg/mL, there was no significant difference in AEs rate per year (p=0.749 and p=0.833, respectively). Also, no significant correlation was observed between IFX doses and AEs rate/year (p=0.159).
Conclusions: Increasing the IFX dose to achieve therapeutic TLs will not increase the risk of AEs in paediatric IBD patients. However, concerns may arise regarding the risk of skin lesions, especially in female CD patients.

BELGIAN WORKING GROUP OF PROCTOLOGY

- M01 -

COMPARABLE PREVALENCE OF ANAL HUMAN PAPILLOMAVIRUS INFECTION AND ABNORMAL CYTOHISTOLOGY IN PRE-EXPOSURE PROPHYLAXIS-USING MSM AND MSM LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS. M. Surmont (1), M. Verheyden (2), J. Gutermuth (2), S. Sahebali (3), M. Goossens (4), S. Allard (5) / [1] UZ Brussel, Jette, Belgium, Gastroenterology, [2] UZ Brussel, Jette, Belgium, Dermatology, [3] UZ Brussel, Jette, Belgium, Pathology, [4] Vrije Universiteit Brussel (VUB), Jette, Belgium, Supporting clinical sciences, [5] UZ Brussel, Jette, Belgium, Internal Medicine and Infectious Diseases.

Introduction: Persistent high-risk HPV (HR-HPV) infection can lead to (pre)cancerous anal lesions. HR-HPV prevalence in HIV-negative MSM and in MSM living with HIV (MSM-HIV) is respectively 41% and 74%. HR-HPV prevalence in Pre-Exposure Prophylaxis (PrEP)-using MSM in Belgium is currently unknown.
Aim: The aim of this study was to determine the prevalence of anal HR-HPV infection and abnormal anal cytohistology in PrEP-using MSM and MSM-HIV. Preliminary data are reported here.
Methods: PrEP-using MSM and MSM-HIV were enrolled in this mono-centric study during appointments at the S-clinic. Patient characteristics, sexual behavior and demographics were collected using a questionnaire, filled in on the day of the anal swab testing. Patients with HR-HPV infection, abnormal cytology or both were subsequently sent for High Resolution Anoscopy (HRA).
Results: We enrolled 149 PrEP-using MSM and 87 MSM-HIV. Quality of anal swabs was sufficient in respectively 95% (n=142) and 82% (n=71) of the participants. HR-HPV prevalence in PrEP-using MSM was comparable with HR-HPV prevalence in MSM-HIV; respectively 74% (n=105) and 74% (n=52) tested positive for at least one HR-HPV (p=1.000). No significant difference in abnormal cytology was seen; 53% (n=75) of PrEP-using MSM and 56% (n=40) of MSM-HIV had either ASC-US, ASC-H, LSIL or HSIL (p=0.664). Until today, 40 PrEP-using MSM and 12 MSM-HIV underwent a HRA. Biopsies were performed in 33 PrEP-using MSM and 12 MSM-HIV. Preliminary results on histology of these lesions show presence of Anal Intraepithelial Neoplasia (AIN) 3 in respectively 20% (n=8) and 25% (n=3) (p= 0.593).
Conclusions: PrEP-using MSM have a similar risk of HPV infection, abnormal anal cytology and biopsy-proven AIN 3 as HIV-positive MSM, which is higher than reported in HIV-negative MSM. ANCHOR showed that treating AIN 3 lesions reduces the incidence of anal cancer in HIV-positive patients, but the risk of progression to anal cancer and thus the need for screening and treatment is to be investigated in the immunocompetent population of PrEP-using MSM.

- M02 -

DOES MINIMALLY INVASIVE LASER ASSISTED TREATMENT OF PILONIDAL SINUS DISEASE LIVE UP TO ITS EXPECTATIONS: A MULTICENTRE STUDY WITH 226 PATIENTS. M. De Decker (1), T. Sels (1), S. Van Hoof (1), Q. Smets (1), T. Hendrickx (2), E. Van Dessel (3), N. Komen (4) / [1] Universiteit Antwerpen / Antwerp University Hospital, WILRIJK (Antwerpen), Belgium, general and abdominal surgery, [2] AZ TURNHOUT, Turnhout, Belgium, general and abdominal surgery, [3] GZA, Wilrijk, Belgium, general and abdominal surgery, [4] Universiteit Antwerpen / Antwerp University Hospital, WILRIJK (Antwerpen), Belgium, Abdominal, Pediatric and Reconstructive Surgery.

Introduction: The minimally invasive character, the possibility to perform under local anaesthesia and the ease to repeat has led to increasing popularity of laser assisted treatment of pilonidal sinus disease. Hereby potentially avoiding prolonged need for medical care at home, incapacity to work and high expenses for patients and society.
Aim: This retrospective, multicentre study aims to evaluate the feasibility of laser assisted treatment for pilonidal sinus disease.
Methods: The patient population is comprised of all patients undergoing laser assisted treatment of pilonidal sinus disease at three Belgian hospitals between January 2017 and December 2021. The required information was collected from the patient's medical file and data was analysed using descriptive statistics in SPSS.
Results: A total of 226 patients were included with a mean follow-up time of 129 days [7-1120]. The healing rate after one laser procedure was 78.8%. Some of these patients were healed by a second or third procedure adding up to an overall success rate of 85.4% after one or more laser procedures. Wound infections were the main postoperative complication (8.0%) of which 5 patients required drainage (2.2%). For 29 patients (12.8%) laser assisted treatment was insufficient, leading to a secondary operation (drainage, excision or flap). At the end of the follow-up, we observed an overall healing rate of 93.4%.
Conclusions: This study shows that laser assisted treatment is feasible for pilonidal sinus disease. The minimally invasive character of this technique makes up for a higher non healing rate compared to other techniques like flap repair.

- M03 -

CRYOTHERAPY BY THE USE OF CRYOPEN® FOR TREATMENT OF NON-MALIGNANT INTRA- AND PERIANAL HPV-RELATED LESIONS. H. Ruymbeke (1), J. Geldof (2), D. De Looze (2) / [1] Vitaz, Sint-Niklaas,

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Introduction: There is no agreed standard of care treatment for non-malignant HPV-related intra- and perianal lesions. These lesions include benign anogenital warts (condylomata acuminata, CA) and anal canal intraepithelial neoplasia (AIN), a precursor stage of anal squamous cell carcinoma. Several techniques are in use with varying efficacy and safety, with little consensus between the guidelines. Cryotherapy is a simple and safe destructive technique with proven efficacy in many skin conditions and anogenital warts, but data on intra-anal CA and AIN are lacking.
Aim: The aim of this study was to fine-tune technical properties and evaluate feasibility, safety and efficacy outcomes of Cryopen®, a new confined N2O based spray cryotherapy technique, in patients with non-malignant intra- and perianal HPV-related lesions.
Methods: This study was a retrospective analysis of all patients with intra- and perianal CA or AIN lesions treated by Cryopen® at a single gastroenterology unit, over a period of 1 year. Feasibility of treatment, safety and efficacy outcomes were reviewed from patient case notes.
Results: Of 47 adult patients included in the analysis, 6 (12.8%) were lost to follow-up. Twenty-five patients (53.2%) were HIV-positive, 3 (6.4%) had a history of solid organ or stem cell transplantation, the remaining 19 patients (40.4%) were immunocompetent. Ten patients (21.3%) only had perianal lesions, 24 (51.1%) only had intra-anal lesions and 13 (27.6%) had both intra- and perianal lesions. Anal cytology was collected using a swab in 39 patients and showed low grade squamous intraepithelial lesion (LSIL= CA and/or AIN 1) in 33 and high grade squamous intraepithelial lesion (HSIL= AIN2 and/or AIN3) in 6 patients. Every visible non-malignant HPV-related lesion was treated with Cryopen® at each treatment session. A total of 155 Cryopen® treatment sessions were performed. Intervals between sessions ranged from 2 to 12 weeks. Complete clinical remission, defined as absence of macroscopic HPV-related lesions, was observed in 35/41 patients (85%). This was achieved after a mean of 3.1 and a median of 2 sessions per patient (range 1-16). Thirty of 35 patients achieved complete clinical remission within 4 months of treatment, only 6/35 needed more than 4 treatment sessions. Although multiple treatment sessions were often necessary to achieve remission, patient compliance was high. Data on safety and adverse events could be collected on 149 treatment sessions in 46 patients. Thirty of 46 patients (65.2%) reported no adverse events after 70 treatment sessions. Sixteen patients (34.8%) reported 35 adverse events after 79 treatment sessions, 34 being mild. Self-limiting mild anal discomfort/pain was seen after 25 sessions (16.8%) in 12 patients, minor anal blood loss after 3 (2.0 %) sessions in 3 patients and mild anal discharge after 6 (4.0%) treatment sessions in 3 patients. Only one serious bleeding (0.7%) was reported, needing intervention. Physician satisfaction on the use of Cryopen® was high.
Conclusions: The present study suggests that Cryopen® is a feasible, easy-in-use, effective and safe technique for treating intra- and perianal non-malignant HPV-related lesions. Patient compliance and physician satisfaction were high. This study can help to standardize future cryotherapy treatment regimens. More prospective, controlled and long-term data are needed to further assess its safety and efficacy, including recurrence rates on the long-term. Further research on treating intra-anal HPV-related lesions should be encouraged.

BELGIAN GROUP FOR DIGESTIVE ONCOLOGY (BGDO)

- O01 -

THE NEED FOR BILIARY DRAINAGE AND ITS IMPACT ON THE ONCOLOGICAL MANAGEMENT OF PATIENTS WITH NEWLY DIAGNOSED BILIARY TRACT TUMOURS. M. Blistein (1), M. Arvanitakis (2), A. Lemmers (2), J. Devière (2), M. Fernandez Y Viesca (2), J.L. Van Laethem (2), D. Blero (3), V. Lucidi (4), D. Germanova (4), J. Closset (4), P. Loi (4), J. Navez (4), A. Demols (2) / [1] Institut Jules Bordet, Brussels, Belgium, Medical Oncology, [2] CUB Hôpital Erasme, Belgium, Gastroenterology and GI oncology, [3] CHR Namur, Namur, Belgium, Gastroenterology, [4] CUB Hôpital Erasme, Belgium, Digestive Surgery.

Introduction: Biliary tracts tumours (BTC) (cholangiocarcinoma and gallbladder adenocarcinoma) are rare tumours with poor prognosis. They are generally diagnosed late at a locally advanced or metastatic stage and may be associated with obstructive jaundice, cholangitis or sepsis. Depending on severity, biliary obstruction should be resolved before the initiation of oncological treatment (surgery or systemic treatment). Endoscopic retrograde cholangiopancreatography is the preferred modality of biliary drainage. Modalities of biliary stenting depend on the type of stricture, the anatomical variations encountered, and the oncological treatment recommended.
Aim: The aim of the study was to assess the impact of endoscopic biliary drainage on: 1/ the oncological management of patients with BTC at the time of diagnosis, and 2/ overall survival. We assessed if the initial drainage and potential related adverse events (AE) would delay surgery or the first cycle of chemotherapy, or even modify the established therapeutic plan after discussion in multidisciplinary oncological meeting (MDOM).
Methods: We conducted a single-center retrospective study (CUB Hôpital ERASME, HUB) collecting data from patients with a newly diagnosed BTC selected from the MDOM registry between 01/01/2016 and 31/08/2021. All patients had histologically confirmed tumours. The patients were divided in group 1 including patients with the need for endoscopic biliary drainage before the initiation of oncological treatment and group 2 including patients who did not require initial drainage. We collected age at diagnosis, gender, type of tumour (cholangiocarcinoma intrahepatic, hilar, distal; or gallbladder cancer), date of histological or cytological diagnosis, histological type and stage of the tumour. Presence of obstructive jaundice associated or not to cholangitis or sepsis at the time of diagnosis were recorded. The first therapeutic plan decided by the MDOM as well as initiation date were noted. For each endoscopic biliary drainage procedure, the type of drainage, the number and type of biliary stents placed (plastic or metal), the type of stricture (hilar or distal) were listed. It was specified whether additional drainage procedures were necessary before the initiation of oncological treatment and the same data was collected (endoscopic and/or percutaneous). We noted the occurrence of procedure-related AE (all grade) as well as mortality. Comparative statistics and survival curves were calculated to define risk factors.
Results: Of 158 patients (57.6 % men, 31% presenting with stage 4 tumour at diagnosis), 76 patients were in group 1 (need for biliary drainage at the time of diagnosis) and 82 in group 2 (no need for biliary drainage at the time of diagnosis). During the initial procedure, 52 patients received plastic and 18 patients self-expandable metal stents (SEMS). Failure during the initial endoscopic procedure requiring a percutaneous approach was encountered in 3 patients and in three patients only tissue acquisition was performed (no stent insertion). In group 1, 39/76 (51%) patients required subsequent drainage procedures (endoscopic or percutaneous) before initiating treatment (in 21/39 patients plastic stents were replaced with SEMS). 49/76 (64%) of the patients in group 1 experienced at least one AE related to the procedure. The time between histological diagnosis and the initiation of oncological treatment was significantly longer in group 1 (50.7 days vs 28.5 days, p=0.005). Furthermore, group 1 encountered significantly more modifications of the therapeutic plan (13.1% vs 2.4%, p=0.002) and 5% of patients died before initiation of oncological treatment (vs 1% in group 2). However, this did not translate into a significant difference in survival between the groups (381 days -group 1 vs 378 days-group 2, p>0.05). After initiation of oncological treatment, 31/76 (40%) patients (group 1) and 18/82 (21%) patients (group 2), required subsequent biliary drainage procedures (endoscopic or percutaneous). The type of tumour (gallbladder adenocarcinoma) and the need for subsequent biliary drainage after initiation of oncological treatment were identified as risk factors of mortality for the whole study population.
Conclusions: In the present retrospective cohort, the need for biliary drainage significantly delays the initiation of oncological treatment of patients with newly diagnosed biliary tract tumours and significantly induces a change in the initial therapeutic plan. Nevertheless, it does not statistically influence overall survival, except if biliary drainage procedures are necessary after the initiation of oncological treatment.

- O02 -

TARGETED DNA METHYLATION SEQUENCING DIFFERENTIATES BENIGN FROM MALIGNANT BILIARY STENOSIS IN BILIARY BRUSH AND BILE FLUID SAMPLES. S. Stoffels (1), S. Cappuyns (2), T. Venken (3), G. Philips (3), W. Laleman (4), S. van der Merwe (5), H. Van Malenstein (5), D. Lambrechts (3), J. Dekervel (6) / [1] KUL - University of Leuven, Leuven, Belgium, Digestive Oncology, [2] University Hospitals Leuven, Leuven, Belgium, Digestive Oncology, Department of Gastroenterology, University Hospitals Leuven, Leuven, Belgium, [3]

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Introduction: Cholangiocarcinoma (CCA) is a highly fatal malignancy of the bile ducts and its diagnosis remains a major clinical challenge, particularly in patients with underlying primary sclerosing cholangitis (PSC). Current detection methods, mostly based on biliary brushing samples, display suboptimal sensitivity and/or specificity, often leading to late diagnosis and increased mortality.
Aim: To identify a diagnostic biomarker using targeted DNA methylation sequencing in a classical training and validation study-design.
Methods: Biliary brushing and bile fluid samples from patients with known malignant versus benign biliary stenoses were prospectively collected during endoscopic retrograde cholangiopancreatography (ERCP). Clinical data including baseline patient characteristics and clinical follow-up data (up to 1 year) were recorded. Samples were subjected to targeted, enzymatic DNA methylation sequencing (EM-seq) using a total of 608,293 capture probes targeting genomic regions known to be hypermethylated in cancer, representing 4.12% of the human genome. Genomic regions differentially methylated in both biliary brush and bile fluid samples were identified using differential methylation analysis. These regions were used to train a 'random forest classification' based prediction model in a training cohort of biliary brush samples, using 10-fold cross-validation. The remaining samples were then used as validation set to test the potential of the methylation score in classifying malignant versus benign samples. Receiver operating characteristic curve analyses were used to evaluate the performance of both the brush-derived and bile fluid-derived methylation scores in differentiating malignant from benign samples.
Results: A total of 70 patients were included between November 2019 and November 2022, of which the majority were men (66%). Mean age was 63 years (range of 30-88) and most patients presented with obstructive jaundice (mean serum total bilirubin 3.58 mg/dL; range 0.19-28.75 mg/dL, mean serum alkaline phosphatase 391.2 U/L; range 32-3547 U/L). Twenty-two patients had a known malignant stenosis, mostly due to CCA (n=11) or pancreatic adenocarcinoma (n=8). Forty-eight patients were known to have benign biliary stenosis, most often caused by ischemic cholangiopathy (n=17). Eight patients had underlying PSC (n=8). In a preliminary analysis of 43 patients comparing 28 benign and 15 malignant biliary stenosis, we identified 669 differentially methylated genomic regions. The average methylation per region in matching brush and bile fluid samples was similar (R2=0.69). Brush-derived methylation scores differentiated between malignant and benign with a specificity of 0.913 and sensitivity of 0.933 (AUC 0.93). Similarly, the methylation scores derived from bile fluid demonstrated a specificity of 0.961 and sensitivity of 0.8 (AUC 0.89).
Conclusions: Targeted DNA-methylation sequencing accurately differentiates malignant from benign biliary stenosis. Bile fluid aspiration during ERCP is a potential alternative when biliary brushing is not feasible. Further validation in larger cohorts is ongoing.

- O03 -

SPECIFIC INHIBITION OF BONE MORPHOGENIC PROTEIN 2 AND 4 (BMP2/4) AS A POTENTIAL THERAPEUTIC STRATEGY FOR ESOPHAGEAL ADENOCARCINOMA.

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Introduction: Esophageal adenocarcinoma (EAC) is a highly aggressive cancer. In Belgium the incidence of this cancer is increasing. Advances in therapy have achieved some incremental improvements in overall outcome of EAC patients, but over- and undertreatment of undefined subgroups of patients might undermine these benefits. Recently we identified three different subgroups based on RNA seq profiles using an unbiased clustering approach and validated the results in the TCGA database (Hoefnagel et al, Cancers 16; 2022). We also found by Geneset enrichment analysis the upregulation of the p38 MAPK signaling pathway in patients in one of the subgroups (Cluster 1). Amongst the important upstream regulators of this pathway are the Bone Morphogenetic Proteins (BMPs), which through non canonical signaling can upregulate this pathway. Previously, we have shown that BMPs are involved in early Barrett's esophagus lesions and possible also overexpressed in EAC (Castillo et al. J Gastrointest Surg 2012).
Aim: We hypothesized that we can target the tumours in cluster 1 by targeting the BMP2 and or4 to decrease signaling via the non-canonical pathways, including the p38 MAPK signaling pathway. For this purpose, we tested our highly specific antibodies against BMP2 and BMP4 (Calpe et al. mAbs 2016; Calpe et al. Mol Cancer Ther 2015). Here we present results from experimental validation of BMP2/4 as a promising target in patients belonging to the most aggressive biological subgroup of EAC.

Methods: To elucidate whether BMP2/4 expression is involved in in EAC we used an RNA sequencing database of 56 EAC treatment naive endoscopic biopsies to investigate if there is a subgroup of cancers with high BMP signaling. We validated results by qPCR and immunohistochemistry in matching tumor samples. Also, we analysed the presence of SMAD4 mutations, the BMP downstream target to investigate non canonical signalling. Next, we used our recently developed effective and highly specific anti-BMP2/4 antibodies to study the effect of inhibition of BMP2/4 on both in vitro as well as in vivo models of EAC.
Results: Using a gene set that was recently published for BMP signaling, we were able to distinguish a subgroup of EAC patients with increased BMP signaling. By IHC we confirmed that 70% of EAC tumours express BMP2/4 at the protein level. We found SMAD4 loss in 10% of cases. We found that patients with high levels of BMP2/4 expression and with SMAD4 mutations tend to have a poorer recurrence-free survival compared to patients with low BMP2/4 expression, which suggests a more aggressive tumour behaviour in BMP4 expressing EAC tumours. Most importantly, inhibition of BMP2/4 function in EAC cells by our recently developed anti-BMP4 antibodies lead to an increase in chemo-sensitivity and a decreased in invasive and migratory capabilities in vitro. Preclinical in vivo studies with a patient-derived tumour xenograft mouse model of an EAC tumour confirmed that anti-BMP2/4 antibodies can effectively reduce tumour growth and synergistically act with chemotherapy agents.
Conclusions: In EAC of cluster 1, we found activation of the p38 MAPK signalling pathway. In a subset of cases this seems to be due to SMAD4 mutations and non-canonical BMP signaling. We hypothesized that targeting BMPs would lead to inhibition of this pathway by inhibiting BMP non-canonical signalling. We showed that inhibition of BMP2/4 function, using our highly specific antibodies, in vitro and in an in vivo model decreases tumor growth and increases chemo sensitivity.

- O04 -

WHOLE-BODY COMPARISON OF 68GA-DOTATATE PET/CT AND PET/MR. N. Ahmadi Bidakhvidi (1), G. Lens (2), V. Vandecaveye (3), S. Grauwels (4), W. Deckers (2), A. Laenen (5), J. Dekervel (6), P. Clement (7), C. Verslype (6), K. Nackaerts (8), E. Van Cutsem (6), M. Koole (9), K. Goffin (1), K. Van Laere (1), C. Deroose (1) / [1] University Hospitals Leuven, KU Leuven, Belgium, Nuclear Medicine and Molecular Imaging, Department of Imaging and Pathology, [2] University Hospitals Leuven, Belgium, Nuclear Medicine, [3] University Hospitals Leuven, Belgium, Radiology, [4] Isala Hospitals, Zwolle, The Netherlands, Radiology, [5] KU Leuven - University of Leuven, Leuven, Belgium, Interuniversity Institute for Biostatistics and Statistical Bioinformatics, [6] University Hospitals Leuven, Belgium, Digestive Oncology, [7] University Hospitals Leuven, Belgium, General Medical Oncology, [8] University Hospitals Leuven, Belgium, Respiratory Oncology, [9] KU Leuven - University of Leuven, Leuven, Belgium, Nuclear Medicine and Molecular Imaging, Department of Imaging and Pathology.

Introduction: Somatostatin receptor (SSTR) positron-emission tomography (PET) is a cornerstone of modern neuroendocrine tumour (NET) management and is used for (re)staging and peptide-receptor radionuclide therapy (PRRT) selection. Hybrid PET/magnetic resonance (MR) is now available for hybrid imaging of NETs, next to PET/computed tomography (CT).
Aim: To determine whether CT or MR with diffusion-weighted sequence is the best hybrid partner for 68Ga-DOTATATE PET. The best hybrid partner was defined as the one with the highest concordance rate of PET findings, as double confirmation of lesions on two different imaging modalities increases the likelihood that these lesions are malignant, ultimately avoiding the need for additional imaging.
Methods: This monocentric, prospective study included patients who received a same-day 68Ga-DOTATATE PET/CT and subsequent PET/MR, for suspicion of NET, (re)staging or PRRT-selection. The union ("PETunion") of malignant lesions detected on PETct and PETmr was considered as a reference standard. Concordance of detection of malignant lesions in an organ was measured between PETunion and CT and PETunion and MR. Bins were used to categorise the number of malignant lesions. The bins contained following ordinal variables: 0, 1, 2-5, 6-10, 11-20, >20 countable and diffuse/uncountable. The difference in number of malignant lesions was obtained as the difference in bin level ("Δbin") between PETunion and CT and PETunion and MR with a Δbin closer to zero implying a higher concordance rate.
Results: Twenty-nine patients were included who received a 68Ga-DOTATATE PET for following indications: 3 suspicions of NET, 7 staging, 16 restaging and 3 PRRT-selection. Primary tumours included 18 GEP-NENs, 7 lung-NETs, 2 meningioma and 2 unknown primaries. Tumour grade comprised 12 grade 1, 9 grade 2 and 1 grade 3. Twenty-four patients had tumoral involvement on PETunion, resulting in a total of 73 organs with tumoral involvement. Organ-based concordance with PETunion was 73% and 40% for MR and CT, respectively ($p<0.0001$). In bone, there was a higher concordance rate for MR compared to CT, 92% and 33%, respectively ($p=0.016$). Overall, a mean Δbin of 0.5±1.1 for PET/MR and 1.4±1.2 for PET/CT ($p<0.0001$) was noted. In liver, a mean Δbin of 0.0±1.1 for PET/MR and 1.7±1.2 for PET/CT was observed ($p=0.0078$). In bone, a mean Δbin closer to zero was observed for PET/MR compared to PET/CT, 0.6±1.4 and 2.0±1.5, respectively ($p=0.0098$).
Conclusions: SSTR PET/MR had a higher organ-based concordance for tumoral involvement and number of malignant lesions, compared to SSTR PET/CT. Specifically, in bone and liver there is a clear added value of hybrid SSTR PET/MR imaging.

CHARACTERISTICS AND MANAGEMENT OF HIGH GRADE GASTROENTEROPANCREATIC NEUROENDOCRINE NEOPLASMS: A BELGIAN ANALYSIS FROM DNET & NETWERK. K. Sarti (1), O. Islam (2), C. Verslype (3), J. Van Laethem (4), H. Rezaei Kalantari (5), J. Janssens (6), A. Hendlisz (7), P. Cuyle (8), G. Demolin (9), J. Decaestecker (10), K. Geboes (11), J. Coche (12), J. Van Ongeval (13), M. Clausse (14), P. Vergauwe (15), A. Bols (16), G. Lambrecht (17), V. Vandersmissen (2), K. Vanden Bulcke (2), L. Annys (2), W. Lybaert (2), M. Peeters (2), I. Borbath (1), T. Vandamme (2) / [1] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Gastroenterology and Digestive Oncology, [2] Antwerp University Hospital, Edegem, Belgium, Oncology, [3] University Clinic Gasthuisberg, Leuven, Belgium, Gastroenterology and Digestive Oncology, [4] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology and Digestive Oncology, [5] CHR VERVIERS, Verviers, Belgium, Oncology, [6] AZ TURNHOUT, Turnhout, Belgium, Gastroenterology and Digestive Oncology, [7] Institut Jules Bordet, Brussels, Belgium, Oncology, [8] Imelda Hospital, Bonheiden, Belgium, Gastroenterology and Digestive Oncology, [9] CHC, Liège, Belgium, Gastroenterology and Digestive Oncology, [10] AZ Delta, Roeselare, Belgium, Gastroenterology and Digestive Oncology, [11] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology and Digestive Oncology, [12] Clinique Saint-Pierre, Ottignies, Belgium, Gastroenterology and Digestive Oncology, [13] AZ Sint-Lucas, Ghent, Belgium, Gastroenterology and Digestive Oncology, [14] Clinique Saint-luc Bouge, Namur, Belgium, Oncology, [15] AZ Groeninge, Kortrijk, Belgium, Gastroenterology and Digestive Oncology, [16] AZ Sint-Jan Brugge-Oostende, Brugge, Belgium, Oncology, [17] AZ Damiaan, Oostende, Belgium, Gastroenterology and Digestive Oncology.

Introduction: Gastroenteropancreatic neuroendocrine neoplasms (GEP-NEN) are a group of heterogeneous neoplasms that arise from neuroendocrine cells. Small intestinal NEN (siNEN), with an incidence of 1.05/100,000 person years and pancreatic NENs (pNEN) with an incidence of about 0.48/100,000 person years are the two most prevalent advanced GEP-NEN (Borbath et al, Eur J Cancer. 2022). GEP-NEN are classified based on their tumour morphology and proliferation rate. While well differentiated GEP-NEN have a relatively long overall survival (OS), High grade GEP-NEN (HG GEP-NEN), comprising both neuroendocrine carcinoma (NEC) and well-differentiated neuroendocrine tumours (NET G3), bear a poorer prognosis Though NET G3 and NEC exhibit many differences in terms of behaviour and chemotherapy sensitivity and data about the optimal management of NET G3 are scarce. The Digestive Neuroendocrine Tumour Registry (DNET: https://www.bgdo.org/clinical-trials/dnet/) of the Belgian group of digestive Oncology (BGDO), and NETwerk - ENETS' centre of excellence in the area of Antwerp - , both have as purpose to improve diagnosis and treatment of NEN by introducing a shared database and allowing clinicians to analyse data from all participating hospitals.
Aim: We retrospectively analysed prospectively collected pathological and clinical data of HG GEP-NEN patients. We aimed to compare general characteristics, prognosis, the value of functional imaging and the treatment of NET G3 vs NEC.
Methods: Data from patients treated in 24 Belgian hospitals were retrieved from the DNET registry and from Oncobase, the NETwerk database. Descriptive analyses and comparisons between the NEN G3 and NEC groups were performed, looking at clinicopathological characteristics, OS and performance of imaging, using R statistics software.
Results: The overall study population is composed of 292 patients (158 DNET and 134 NETwerk patients) with 40% female patients; 222 (75.8%) were NEC, of which 56 small-, 56 large-cell, 3 mixed and others unknown; 66 (22.5%) were NET G3, and 5 non-specified. Mean age at diagnosis was 67 (range 23-88) and 58 years (range 19-90) for NEC and NET G3, respectively. Median Ki67 was 70% (range 21-100%): 30% (range 21-100%) in the NET G3 group and 80% (range 21-100%) in the NEC group. Most frequent primary locations were pancreatic (32%) and colorectal (21%). 78% of the total population had stage 4 disease at diagnosis. Median OS in the total population was 17.4 months (95% Cl: 14.7 - 21.4) and was significantly higher in NET G3 compared to NEC, with a median OS of 39,1 (95%CI: 33-77.4) and 13.1 (95% CI: 10.5-16) months respectively, $p<0,05$. Overall, patients with a Ki67 value <55% showed a better OS compared to those with a Ki67 > 55%, (median OS for Ki67 < 55% 31 months (95% CI: 24,5 -39,7), median OS for Ki67> 55% 12.2 months (95% CI: 10 - 16,3), $p <0,05$. This cutoff was shown to be of relevance within subgroups of NET G3 and NEC as well. Somatostatin receptor imaging (SRI) was positive in 77/95 patients (81%). FDG-PET imaging was positive in 147/156 (94%). 68 patients had both of which 48 were positive for both, 4 patients showed only SSTR expression and 16 had only FDG uptake. Patients with positive SRI had a better OS compared to patients with negative SRI (median OS 39 months in SSR positive group vs 24.4 months in SRI negative, $p<0.05$). 108 (37%) patients underwent surgery. Chemotherapy (Platinum-etoposide) as first line was given in 165 patients (150/222 NEC, 15/66 NET G3); 98 patients received second-line treatment, consisting mainly of 5 FU-based regimens (52 patients) and platinum/etoposide rechallenges (23 patients).
Conclusions: We report the largest cohort of HG GEP-NEN patients studied in Belgium. In line with previous results, we show that OS was significantly influenced by differentiation grade, proliferation index. More interestingly, our results suggest that SRI positivity may be correlated with a longer OS, both in NET G3 and NEC. Based on these results, we suggest performing SRI also in NEC.

- O06 -

NEOADJUVANT IMMUNOTHERAPY FOR MICROSATELLITE INSTABILITY HIGH LOCALLY ADVANCED RECTAL CANCER. C. Claeys (1), G. Mertens (2), K. Haustermans (3), A. Wolthuis (4), A. D'Hoore (5), R. Dresen (6), F. Van Herpe (2), S. Tejpar (2), E. Van Cutsem (2), J. Dekervel (2) / [1] Univeristy Hospitals Leuven, Leuven, Belgium, Department of Gastroenterology/Digestive Oncology, [2] University Hospitals Leuven, Belgium, Department of Gastroenterology/Digestive Oncology, [3] University Hospitals Leuven, Belgium, Department of Radiation Oncology, [4] Univeristy Hospitals Leuven, Leuven, Belgium, Department of Abdominal Surgery, [5] University Hospitals Leuven, Belgium, Department of Abdominal Surgery, [6] University Hospitals Leuven, Belgium, Department of Radiology.

Introduction: Immune checkpoint inhibition (ICI) targeting programmed death-1 (PD-1) is the standard treatment for metastatic microsatellite instability high (MSI-H)/ mismatch repair deficient (dMMR) colorectal cancer, producing long-lasting responses. Emerging evidence suggests an important role for neoadjuvant ICI in local and locoregional disease, especially in anatomical regions associated with high surgical morbidity.
Aim: Here, we report single-center data of the clinical course and outcome of all patients with MSI-H locally advanced rectal cancer (LARC) treated with off-label ICI as part of their neoadjuvant treatment.
Methods: We retrospectively assessed all records from patients with MSI-H LARC who received neoadjuvant ICI between 06/2020 and 11/2022. Patients received exhaustive information about the non-standard approach and signed informed consent for off-label drug use. Duration of ICI treatment before first multimodal evaluation as well as result of this evaluation was recorded. A complete clinical response was defined as the absence of residual disease on digital examination, endoscopic evaluation and rectal MRI.
Results: Six unique patients were identified. First evaluation has not occurred yet for one patient and will be discussed at the meeting. Four patients received a short course of radiotherapy (5x5 Gy) prior to the administration of immunotherapy and two patients received up-front ICI without radiotherapy. Median number weeks of ICI treatment before first evaluation was 10,6 (range, 5.6-14.9). Complete clinical response was observed in three patients at first evaluation. All three patients currently remain in remission without surgery and a follow-up time of 24,6, 14,1 and 11,7 months. Partial clinical response was observed in two patients. One patient underwent a transanal total mesorectal excision (ypT2 N0). The other patient responding to neoadjuvant ICI continued treatment after the first evaluation with the aim to achieve a clinical complete response.
Conclusions: In this case series of six patients receiving neo-adjuvant ICI for MSI-H LARC +- short course radiotherapy, clinical responses were noted in all evaluable patients. After a median of 10, 6 weeks ICI treatment, three patients had a complete clinical response followed by a watch and wait strategy. Two patients had a partial response of which one underwent surgery. Longer follow-up data will be presented at the meeting. The role of neoadjuvant immunotherapy in MSI-H LARC is promising, although more prospective clinical trials with a longer follow-up are required to establish its exact modalities and value.

- O07 -

ISOTOXIC HIGH-DOSE STEREOTACTIC BODY RADIOTHERAPY VERSUS CHEMORADIOTHERAPY FOR LOCALIZED PANCREATIC CANCER: A SINGLE CENTER EVALUATION. M. Manderlier (1), J. Navez (2), M. Hein (3), J. Engelholm (4), J. Closset (2), M. Bali (5), D. Van Gestel (1), L. Moretti (1), J. Van Laethem (6), C. Bouchart (1) / [1] Institut Jules Bordet, Brussels, Belgium, Radiation oncology, [2] Hopital Universitaire Erasme, Brussels, , Belgium, Hepato-biliary-pancreatic surgery, [3] Université Libre de Bruxelles, Belgium, Faculty of Medicine, [4] Hôpitaux Iris Sud, Brussels, Belgium, Radiology, [5] Institut Jules Bordet, Brussels, Belgium, Radiology, [6] Hopital Universitaire Erasme, Brussels, Belgium, Gastroenterology, Hepatology and Digestive Oncology.

Introduction: Pancreatic cancer is a highly aggressive solid tumour with poor prognosis. The overall survival rate at 5 years is only 7%, an oncologic surgical resection being the only potentially curative treatment. To increase this probability and better select the patient for surgery, the use of neoadjuvant therapies [including chemoradiotherapy (CRT) or stereotactic body radiotherapy (SBRT) as radiotherapeutic modality) has been explored and the exact neoadjuvant therapeutic sequence still needs to be validated.
Aim: In lack of direct comparative evidence of isotoxic high-dose SBRT (iHD-SBRT), we compared the clinical outcomes of patients treated for localized pancreatic ductal adenocarcinoma (PDAC) by iHD-SBRT with those of patients treated with conventional CRT in the same tertiary cancer center.
Methods: From January 2006 to January 2021, all consecutive biopsy-proven borderline/locally advanced (BR/LA) patients treated with iHD-SBRT (35Gy in 5 fractions with a simultaneous integrated boost up to 53Gy; January 2018 - January 2021) or conventional CRT (45-60Gy in 25-30 fractions; January 2006 – December 2017) as a primary neoadjuvant or definitive treatment strategy were retrospectively included. In the CRT group, a clinical target volume was generated using an expansion of 1 cm from the gross tumour volume (GTV) and completed by the elective nodal regions around the superior mesenteric vessels, portal vein and celiac axis. For the iHD-SBRT group, an internal target volume accounting for respiratory motion was created for the GTV and the tumour-vessel interface structure (whole

circumference of abdominal vessels in contact with GTV). iHD-SBRT was integrated in a total neoadjuvant strategy, before surgical exploration and after induction chemotherapy by modified FOLFIRINOX for ideally 6 cycles. The median overall survival (mOS) was further evaluated trough uni- and multivariate analyses. The median progression free survival (mPFS) and the 1-year local control (1y-LC) were also reported.
Results: 82 patients (41 in each group) were included. The main baseline characteristics of both groups were comparable. Significant differences in terms of duration and type of induction chemotherapy, and oncological resection rates were identified between the groups. Induction chemotherapy consisted of mFFX or Gem-Np for, respectively, 29.3% and 100% of the CRT and the iHD-SBRT cohort. For the rest of the CRT cohort, the induction chemotherapy consisted of gemcitabine alone in 26.8%, gemcitabine combined with another agent (cisplatin, 5FU, etc.) in 29.3%; 24.4% had no induction chemotherapy. The median number of chemotherapy cycles was 3 (IQR 0–5) in the CRT group and 7 (IQR 6–8) in the iHD-SBRT group ($p < 0.001$). The median duration of induction chemotherapy was 2.1 months (IQR 0.8–3.3) for CRT and 3.7 months (IQR 2.6–4.6) for iHDSBRT ($p < 0.001$). An oncological resection was performed in 9.8% and 46.3% of the cases for the CRT and iHD-SBRT groups, respectively ($p < 0.001$). After a median follow-up of 19.7 months, the mOS (15.9 vs 22.5 months, p<.001), 2y-OS (10.0 vs 43.9%, p=.001), mPFS (11.5 vs 16.7 months, p=.011) and 1y-LC (39.3 vs 75.8%, p=.004) were all in favour of the iHD-SBRT group. Through univariate Cox regression analysis, the following factors were significantly associated with the mortality risk: number and duration of induction chemotherapy cycles, type of induction chemotherapy and radiotherapy received, and oncological resection. A multivariate Cox regression analysis for the mortality risk associated with radiotherapeutic treatments was performed. After adjusting for the main significant confounding factors highlighted during univariates analysis, multivariate analysis demonstrated that unlike CRT, iHD-SBRT was significantly associated with a lower mortality risk for BR/LA PDAC (HR 0.39 [CI95% 0.18 – 0.83], p=.014).
Conclusions: iHD-SBRT is a promising radiotherapeutic option and may offer an improvement in mOS in comparison with conventional CRT for localized PDAC. Further studies are required to confirm the exact role of iHD-SBRT and the optimal therapeutic sequence for the treatment of localized PDAC. For this purpose, our group launched the randomized phase II STEREOPAC trial [NCT05083247] aiming to compare mFFX alone versus mFFX + iHD-SBRT as neoadjuvant strategies in 256 patients with borderline resectable PDAC.

- O08 -

PROSPECTIVE FOLLOW UP OF LIVER STIFFNESS AND CONTROLLED ATTENUATION PARAMETER MEASUREMENTS BY FIBROSCAN AS NONINVASIVE TOOL FOR THE EARLY DETECTION OF OXALIPLATIN-INDUCED HEPATOTOXICITY IN COLORECTAL CANCER PATIENTS. B. Vos (1), J. Rigaux (2), S. Evrard (2), A. Huard (3) / [1] CHIREC Braine l'Alleud, Braine l'Alleud, Belgium, Gastroenterology and digestive oncology, Chirec cancer institute, [2] CHIREC Braine l'Alleud, Braine l'Alleud, Belgium, Gastroenterology, [3] CHIREC Braine l'Alleud, Braine l'Alleud, Belgium, Internal medicine.

Introduction: Oxaliplatin remains an essential component of many chemotherapy protocols for colorectal cancer; however, neurotoxicity and hepatotoxicity may be dose-limiting. The gold standard for the diagnosis of oxaliplatin-induced hepatotoxicity is liver biopsy, which is invasive and costly.
Aim: The aim of our study is to evaluate the clinical interest of noninvasive Fibroscan use to follow hepatotoxicity induced by Oxaliplatin in colorectal cancer patients.
Methods: Between 1st January 2021 to 30th April 2022, patients diagnosed with colorectal cancer and planned to receive at least 6 months of chemotherapy containing oxaliplatin were included in a prospective monocentric study. Liver stiffness measurements for fibrosis and controlled attenuation parameter (CAP) for steatosis by Fibroscan were performed at baseline and 6 months after starting oxaliplatin based regimen. Comparison between median liver stiffness measurements and CAP were compared between patients using Student t-test.
Results: 56 consecutive patients with colorectal cancer were enrolled during the study period. Median age (min-max) at diagnosis was 64 (37-82) years with a male predominance (56%). 26 patients (46%) were metastatic at diagnosis, including 23 patients (41%) with synchronous metastatic liver. 7 were excluded for aberrant result of Fibroscan due to right liver metastasis and 1 patient excluded for alcoholic cirrhosis at diagnosis. Median number of chemotherapy sessions between baseline Fibroscan and 6 months Fibroscan evaluation was 12 (9-13) sessions. In 48 patients treated by 6 months of Oxaliplatin regimen, median (min-max) stiffness increased significatively compared to baseline: 6.4 kPa (3.2-13.5) at 6 months vs. 5.8 kPa (2.2-12.5) at baseline, p=0.0036. Median CAP was not modified by 6 months of oxaliplatin-based chemotherapy (p=0.303) but median baseline CAP (min-max) was significantly higher in obese patients (body mass index >30 kg/m2, n=12 (25%)): 225 dB/m (138-324) vs. 284 dB/m(192-376), p=0.028.
Conclusions: Fibroscan can overestimate liver fibrosis in case of voluminous right liver metastasis. Measurement of liver stiffness using Fibroscan could be an effective non-invasive tool to predict oxaliplatin-induced hepatotoxicity in colorectal cancer patients.

PROSPECTIVE COMPARISON OF [18F]ALF-NOTA-OCTREOTIDE PET/MRI TO [68GA]GA-DOTATATE PET/CT IN NEUROENDOCRINE TUMOR PATIENTS. L. Boeckxstaens (1), E. Pauwels (2), V. Vandecaveye (3), W. Deckers (4), F. Cleeren (5), J. Dekervel (6), T. Vandamme (7), K. Serdons (4), M. Koole (8), G. Bormans (5), A. Laenen (9), P. Clement (10), K. Geboes (11), E. Van Cutsem (6), K. Nackaerts (12), S. Stroobants (13), C. Verslype (6), K. Van Laere (4), C. Deroose (4) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Nuclear Medicine, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Nuclear Medicine and Molecular Imaging, Department of Imaging and Pathology, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Radiology, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Nuclear Medicine and Molecular Imaging, [5] KUL - University of Leuven, Leuven, Belgium, Radiopharmaceutical Research, Department of Pharmacy and Pharmacology, [6] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Digestive Oncology, [7] University of Antwerp, Antwerp, Belgium, Center for Oncological Research (CORE), [8] KUL - University of Leuven, Leuven, Belgium, Nuclear Medicine and Molecular Imaging, [9] KUL - University of Leuven, Leuven, Belgium, Leuven Biostatistics and Statistical Bioinformatics Center, [10] University Hospitals Leuven (UZLeuven), Leuven, Belgium, General Medical Oncology, [11] University Hospital Ghent (UZ Gent), Gent, Belgium, Digestive Oncology, Department of Gastroenterology, [12] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Respiratory Oncology, [13] University of Antwerp, Antwerp, Belgium, Nuclear Medicine.

Introduction: Most neuroendocrine tumours (NETs) are characterized by an overexpression of the somatostatin receptor (SSTR), predominantly subtype 2, making it an ideal target for molecular imaging and radionuclide therapy with somatostatin analogues (SSAs). To date, the gold standard for SSTR imaging is positron emission tomography (PET) with [68Ga]Ga-DOTA-SSAs such as [68Ga]Ga-DOTANOC, [68Ga]Ga-DOTATOC or [68Ga]Ga-DOTATATE. However, the use of 68Ge/68Ga-generators for the production of the radionuclide 68Ga has its inherent clinical challenges such as limited availability, high associated costs and low activity yield per elution. Fluorine-18-labeled SSAs could represent a valid alternative SSTR imaging as their logistical advantages allow to overcome these challenges. In a recent prospective multicenter and multi-arm trial (NCT04552847), we showed in a first arm with PET/CT that [18F]AlF-NOTA-octreotide ([18F]AlF-OC) was superior compared with [68Ga]Ga-DOTA-SSA: of 4709 different PET/CT based tumour lesions, 3454 (73.35%) were detected with [68Ga]Ga-DOTATATE/NOC compared to 4278 (90.85%) with [18F]AlF-OC ($p<10-5$). We here report results of the second arm, using magnetic resonance imaging (MRI) in a PET/MRI setting. [18F]AlF-OC lesions were identified and compared to simultaneously acquired MRI.

Aim: One particular aim was to determine the MRI correlate of [18F]AlF-OC lesions, especially those only detected by [18F]AlF-OC and not by [68Ga]Ga-DOTA-SSA ("incremental lesions").

Methods: Ten patients with histologically confirmed NET and a routine clinical [68Ga]Ga-DOTATATE PET/CT, performed within an interval of median 13.5 days (range: -8 to +47 days), were included. Patients underwent a whole-body PET/MR, two hours after IV injection of 4 MBq/kg [18F]AlF-OC. An unblinded consensus read of the PET was performed by two experienced readers to score tumour lesions. These PET lesions were checked for a corresponding lesion on MRI images by an experienced radiologist, unblinded for the tracer used. If MRI confirmed the PET lesion to be a NET lesion, it was defined as an MRI-confirmed lesion. The percentage of MRI-confirmed lesions from the total amount of PET lesions was determined and other causes of [18F]AlF-OC uptake on MRI were recorded. The detection ratio (DR), i.e. the fraction of PET lesions detected on a scan compared to the union of PET lesions of both scans, was determined for each scan. The differential detection ratio (DDR; difference in DR between [18F]AlF-OC and [68Ga]Ga-DOTATATE) per patient was calculated. After correlation with MR, the DR and the DDR were also determined for the MRI-confirmed NET lesions. Tracer uptake was evaluated by comparing SUVmax and tumour-to-background ratios (TBRs) in concordant lesions.

Results: In total, 195 different lesions were detected, 167 with [68Ga]Ga-DOTATATE and 193 with [18F]AlF-OC. A trend towards a higher DR with [18F]AlF-OC compared to [68Ga]Ga-DOTATATE (99.1% vs 91.4%) was observed, resulting in a mean DDR of 7.7% (95% CI -0.4 – 15.8) in favor of [18F]AlF-OC. Although not significantly superior (P=0.0595) compared with [68Ga]Ga-DOTATATE, it was definitely meeting the criteria for non-inferiority (P=0.0001). Out of these 193 lesions MRI showed a corresponding lesion in 185 lesions of which 178 (96.2%) were NET lesions and thus considered as MRI-confirmed NET lesions. Seven lesions (3.8%) were caused by another SSTR positive entity, like schwannomas, fibromyomas and a haemangioma. The mean DR for the MRI-confirmed NET lesions was 98.9% with [18F]AlF-OC and 91.9% with [68Ga]Ga-DOTATATE resulting in a mean DDR of 7.1% in favour of [18F]AlF-OC, significantly non-inferior (P=0.0003) compared to [68Ga]Ga-DOTATATE. In total 33 incremental lesions were identified by [18F]AlF-OC, of which 30 (91%) were confirmed by MRI as true NET lesions. Of the remaining three lesions, one was diagnosed as a NET lesion during further follow up, one was caused by SSTR-expression in a schwannoma, and one remains undetermined. No significant differences in mean SUVmax or TBR were observed between [18F]AlF-OC and [68Ga]Ga-DOTATATE.

Conclusions: [18F]AlF-OC performed non-inferior to [68Ga]Ga-DOTATATE and incremental lesions were confirmed by MRI in more than 90% of lesions as true positives. This further validates [18F]AlF-OC as an option for clinical practice SSTR PET.

- O10 -

FEASIBILITY AND EFFICACY OF HEPATIC ARTERIAL CHEMOTHERAPY FOR LIVER METASTASES OF COLORECTAL CANCER: A SINGLE CENTER RETROSPECTIVE STUDY. C. Wang Zhang (1), J.L. Van Laethem (2), G. Verset (3), V. Lucidi, (4), D. Germanova (4), I. Tancredi, (5) / [1] Hôp. Iris Sud Bracops, Bruxelles, Belgium, Medecine interne [2] CUB Hôpital Erasme, Belgium, Service de Gastro-Entérologie/Oncologie Digestive [3] CUB Hôpital Erasme, Belgium, Service de Gastro-Entérologie/Oncologie Digestive, [4] CUB Hôpital Erasme, Belgium, Chirurgie Digestive, [5] CUB Hôpital Erasme, Belgium, Radiologie Interventionnelle.

Introduction: Hepatic arterial infusion chemotherapy (HAI) associated with systemic chemotherapy is a treatment option in the management of colorectal liver metastases (CRLM) and shows promising results both in palliative care and adjuvant chemotherapy after liver metastases resection.
Aim: Our aim is to evaluate its feasibility, safety, efficacy of HAI-oxaliplatin with systemic chemotherapy.
Methods: Between 2014 and 2022, single-centre consecutive patients who receive HAI-oxaliplatin plus systemic chemotherapy were retrospectively analysed at Erasme University Hospital.
Results: Forty-one patients were included and divided into two groups: adjuvant group (n=18) and "palliative" group (n=23) who previously received a median number of one systemic chemotherapy (83% including oxaliplatin). The objective response rate (ORR) and tumour control rate (TCR) of the palliative group were respectively 50% and 70% with secondary resection in 20% of cases. For this group, the median OS was 26 months. For the adjuvant group, after resection of a median number of four metastases and adjuvant treatment with HAI-oxaliplatin, the 2-year OS and liver PFS were 86% and 56% and more than 50% of these patients are still alive. Poor prognostic factors regarding OS were the presence of extrahepatic metastases (P=0.004), the number of pre-CIAH chemotherapy lines (P=0.038), and the diameter of CRLM (P=0.010). Finally, CIAH is feasible and well-tolerated, with patients not experiencing major side effects apart from altered liver tests.
Conclusions: HAI-oxaliplatin is a feasible, effective and well-tolerated treatment and show promising results on the impact of OS and PFS. Our results are in the range of published data and confirm the interest that HAIC may bring added value to the management of CRLM.

- O11 -

POSTOPERATIVE HEPATIC ARTERIAL INFUSION PUMP CHEMOTHERAPY AFTER RESECTION OF COLORECTAL LIVER METASTASES. R. Brawermann (1), G. Verset (2), A. Bohlok (3), D. Germanova (4), V. Donckier (3), F. Tannouri (5), J. Van Laethem (2), V. Lucidi (4) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Surgery, [2] CUB Hôpital Erasme, Belgium, Gastroenterology, [3] CUB Institut Jules Bordet, Brussels, Belgium, Surgery, [4] CUB Hôpital Erasme, Belgium, Surgery, [5] Hopital Erasme, ULB, Belgium, Radiology.

Introduction: Despite curative-intent surgical resection, most patients with multinodular colorectal liver metastases (CRLM) will recur and postoperative chemotherapeutic treatment is debated for reducing these recurrences. Hepatic arterial infusion pump chemotherapy (HAIPC) allowing higher doses of cytotoxic agents directly in the liver also remains a matter of discussion. This study aims to evaluate the feasibility and safety of postoperative HAIPC in patients who underwent surgery for multiple CRLM and to evaluate its potential survival benefit as compared with a control group without HAIPC.
Aim: The primary objective was to determine the safety and feasibility of postoperative HAIP chemotherapy for patients undergoing a curative-intent liver surgery of multinodular (≥4) CRLM. The secondary objective was to analyse the influence of HAIPC on survival outcome in these patients.
Methods: Consecutive patients undergoing curative-intent resection of CRLM between 2014 and 2020 were retrospectively analysed. Inclusion criteria were presence of at least four or more CRLM presenting liver only metastatic disease. HAIPC related morbidity and feasibility (at least one cycle administered) were analysed and survivals among HAIPC and the control group were compared. A propensity score matching (PSM) 1:1 was used to compare groups reducing bias of selection.
Results: Seventy-two patients matched the inclusion criteria. Sixteen of them (22%) were treated with HAIPC and 56 (78%) had either systemic chemotherapy 15 (21%) or no postoperative treatment 41 (57%). Four (25%) patients experienced HAIPC related complications of which 3 had to stop HAIPC after the second cycle. The disease-free survival (DFS) was similar in both groups with a median of 9 and 6 months respectively for the HAIPC and control groups (p=0,3). Overall survival (OS) was 63 (CI: 35-91) months for the HAIPC group compared to 39 (CI: 31-47) months for the control group (p=0,07).
Conclusions: Our study showed that HAIPC after resection of multiple CRLM is safe and feasible. Despite no benefit in DFS, HAIPC seems to improve OS. The role of HAIPC in this context should be studied and clarified in randomized controlled clinical trials.

- O12 -

S100A14 AS A POTENTIAL BIOMARKER DISTINGUISHING HYPERPLASIC POLYPS FROM SESSILE SERRATED LESIONS. P. Adam (1), C. Salée (1), F. Quesada Calvo (1), A. Merli (1), C. Massot (2), N. Blétard (3), J. Somja (3), D. Baiwir (4), G. Mazzucchelli (5), C. Coimbra Marques (6), P. Delvenne (3), E. Louis (2), M. Meuwis (2) / [1] University of Liege, GIGA-R, Liège, Belgium, Laboratory of Translational Gastroenterology, [2] University of Liège and CHU of Liège, LIEGE, Belgium, Laboratory of Translational Gastroenterology and Hepato-Gastroenterology and Digestive Oncology, [3] University Hospital CHU of Liège, Belgium, Pathological Anatomy and Cytology, [4] University of Liege, GIGA-R, Liège, Belgium, GIGA Proteomics Facility, [5] University of Liège, Liège, Belgium, Laboratory of Mass Spectrometry, [6] University Hospital CHU of Liège, Belgium, Abdominal Surgery Department.

Introduction: Serrated lesions are mucosal colorectal lesions regrouping hyperplastic polyps (HP) considered harmless and serrated sessile lesions (SSL) which lead to colorectal cancer (CRC) in about 30-35% of the cases (Trovato et al., World J Gastroenterol 2021). The epithelial transformation leading to SSL follows the serrated pathway which is characterized by features as the BRAF mutations as BRAFV600E, micro-satellite instability and hyper methylation of CpG islands. Despite such SSL features and due to the flat or depressed shape of SSL, the discrimination of HP and SSL remains challenging both at the endoscopic and the histological level. Up to date, no histological marker is available to help in this specific diagnosis.
Aim: This work aims at comparing by proteomics profiles of SSL and adenomas and to highlight potential element of the serrated pathways and assess the potential of specific proteins as biomarkers for histological discrimination of SSL from HP.
Methods: We analysed FFPE tissue of 20 controls (normal margin of patients with diverticular disease) sand 57 colonic lesions: adenoma (n=45) and SSL (n=12) after reviewing by two trained pathologists. After enrichment of epithelial cells by macrodissection and pool composition, we used FFPE-FASP kit (Expedeon) before peptide digests preparation and differential label free proteomics. We performed protein identification/quantitation and differential analysis using the MaxQuant and Persues programs. After a specific strategy of selection, with proteins differentially distributed within these lesions, we focused on one protein associated with SSL and confirmed its specific tissue distribution by immunohistochemistry (IHC) on an independent cohort including normal margin of patients with diverticular disease (n=9), HP (n=26), SSL (n=27), low grade adenomas (n=8), high grade adenomas (n=10) and CRC at pT1NM) (n=10). BRAFV600E mutational status of all the tissues was obtained. A semi-quantitative IHC scale (0 to 4) was used by two scorers to assess this protein tissue distribution. Anova with Dunn post-hoc test was used to assess for its discriminating power between groups.
Results: We identified 5592 proteins with high confidence after search on the Human proteins uniport database. Thanks to the differential analysis results and additional criteria originated from literature (Sohier et al., J Pathol, 2020), we selected 14 proteins showing a significant difference in abundance in SSL versus normal tissues and adenomas. The Protein S100-A14 (encoded by S100A14), selected for IHC characterisation in the confirmatory independent cohort increased significantly in SSL compared to normal, pre-cancerous and CRC tissues. But more importantly an increased intensity was detected in SSL compared to HP, at the upper and middle part of the crypts suggesting an association with differentiating and mature colonic cells in SSL.
Conclusions: This retrospective study comparing SSL, low/high grade adenomas and CRC at pT1NM confirms the increased distribution of S100A14 observed by proteomics. The higher IHC intensity of the S100A14 observed in SSL compared to HP, suggests a potential as histological biomarker which nevertheless requires other confirmations. Other markers candidates are still under study in order to disclose any specific association with SSL and could be useful in addition to S100A14 IHC for SSL form HP discrimination. Functional studies are also needed to understand the tissue distribution obtained with S100A14 in these lesions and its implication in the serrated pathways.

- O13 -

EVALUATION OF LOCO-REGIONAL RECURRENCES USING DEFORMABLE IMAGE REGISTRATION AFTER ISOTOXIC HIGH DOSE STEREOTACTIC BODY RADIOTHERAPY IN LOCALIZED PANCREATIC CANCER. M. Manderlier (1), C. Bouchart (1) / [1] Institut Jules Bordet, Brussels, Belgium, Radiation Oncology.

Introduction: Pancreatic cancer is a highly aggressive solid tumour with an overall survival rate at 5 years of 7%. A complete oncologic surgical resection being the only potentially curative treatment, neoadjuvant therapies (including radiotherapy and/or chemotherapy) have been explored to increase this probability. Although stereotactic body radiotherapy (SBRT) has showed promising results and may provide some advantages over chemoradiotherapy (CRT), SBRT treatments imply the use of smaller target volume not taking in account the elective nodal zones.
Aim: To perform an imaging-based clinical evaluation of the loco-regional recurrence (LRR) pattern after isotoxic high dose stereotactic body radiotherapy (iHD-SBRT) for localised pancreatic cancer using deformable image registration (DIR).

Methods: From January 2018 to January 2021, patient with borderline/locally advanced (BR/LA) pancreatic adenocarcinoma were included. Cases without clearly identified LRR after a total neoadjuvant strategy were excluded. The neoadjuvant treatment was composed of induction chemotherapy (modified FOLFIRINOX) followed by iHD-SBRT (35Gy in 5 fractions with a simultaneous integrated boost up to 53Gy) and surgical exploration (if operable and no progression). No elective nodal irradiation was used for iHD-SBRT and a tumour-vessels interface (TVI) structure was created by including the whole circumference of major abdominal vessels in direct contact with the gross tumour volume (GTV). During the follow-up, LRR were identified on CT or MRI. The same imaging modalities of LRR and RT-planning were imported in MIM (v7.1.5, MIMvista Inc, Cleveland, OH, USA), delineating the following structures: major abdominal great vessels, pancreas, primary tumour and LRR (only on the latter image set). A tailored DIR procedure was performed and validated prior the back propagation of the LRR to the initial imaging using: DICE similarity coefficient [DICE] for volumetric assessment, Hausdorff distance 95% [HD95%] and mean distance to agreement [MDA], Jacobian determinant [JD} was used for DIR plausibility and a visual inspection as qualitative assessment. Finally, the 35Gy isodose line (ID35) of the initial plan was used to classify the back-propagated LRRs as: in-field (IF) if more than 50% of the recurrence volume is in the ID35, marginal (M) if the recurrence volume in the ID35 is between 20 and 50% and out-of-field (OF) if less than 20% of the recurrence volume is in the ID35.
Results: Among 41 patients treated by iHD-SBRT for localized pancreatic cancer, a LRR was clearly identified in 17 patients (ten on CT and seven on MRI). The tailored DIR workflow confirmed plausible correspondence between the two image sets. Great Vessels offered a reliable guide for DIR adjustments. DICE showed good and moderate agreement for Great Vessels and pancreas, respectively. Mean Jacobian showed plausible DIR, with values of 0.94 and 0.89 for Great Vessels and pancreas, respectively. Visual inspection offered a clinically satisfactory agreement within the region of interest. The majority of the LRR were classified as OF (n=9), while four cases were identified as IF (primitive pancreatic cancer progression) and the remaining four as marginal recurrences close to major abdominal vessels (one close to the superior mesenteric artery, one close to the celiac artery and two close to the hepatic hilum).
Conclusions: Imaging based evaluation of loco-regional recurrence is an important part of the assessment of a neoadjuvant treatment strategy including iHD-SBRT for localized pancreatic cancer. Based on the tailored deformable image registration, four marginal LRR occurred, close to the vessels around the primary tumour. This highlights the need to include the whole circumference of the major abdominal vessels in direct contact with the GTV in the TVI structure, with at least 5mm margin on both sides of the GTV, in order to further minimize the risk of marginal LRR after iHD-SBRT.

- O14 -

CLINICAL AND MOLECULAR VARIABLES ASSOCIATED WITH RESPONSE TO CHECKPOINT INHIBITORS IN PATIENTS WITH MSI-H METASTATIC COLORECTAL CANCER: A RETROSPECTIVE COHORT STUDY.
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Introduction: Deficient mismatch repair (dMMR)/microsatellite-instability–high (MSI-H) is an established biomarker for response to immune checkpoint inhibitors (ICIs) in metastatic colorectal cancer (mCRC). However, 30% of ICI-treated dMMR/MSI-H mCRC patients have primary resistance or early progression, while others benefit from exceptionally long-lasting responses and survival. Therefore, prognostic and predictive markers beyond MMR/MSI status are needed for clinical decision making.
Aim: Identify clinical and molecular variables associated with durable ICI-induced disease control and improved outcomes.
Methods: In a retrospective cohort study, all MSI-H/dMMR mCRC patients treated with ICI at the University Hospitals Leuven between June 2014 and May 2022 were reviewed. Patients were divided into two groups based on clinical response. Patients with documented disease progression at any time during follow-up were defined as progressors, while non-progressors demonstrated durable disease control with at least 12 months of follow-up. Kaplan-Meier curves were generated and compared between groups using the log-rank test. Differences in clinicopathological characteristics between progressors and non-progressors were assessed using uni- and multivariate logistic regression analysis. Additionally, uni- and multivariate cox regression analysis was used to identify parameters associated with improved survival (OS).
Results: Overall, 84 patients with dMMR/MSI-H mCRC were included, treated with anti-programmed-death (ligand)-1 (PD(L)-1) monotherapy (n=64) or anti-PD-1/anti-cytotoxic T-lymphocyte antigen 4 combination (n=20). Patients were mostly female (56%), with predominantly right sided colon tumors (66%) and a mean age of 64 years (range 30-92) prior to start of therapy. Median time of follow-up was 39 months. Progressive disease after start of ICI occurred in 37 (44%) patients, but only in 11 (19%) patients with disease control at 12 months. As expected, median overall survival was markedly different between progressors and non-progressors (17 months vs not reached; 95% CI 8m – 42m; $p<0.0001$). In multivariate analysis, progressors were more likely to have lung metastases ($p=0.049$) and less likely to experience immune-related adverse events ($p=0.047$). In the total cohort, median OS was 80 months (95% CI 44m – not estimable) and improved outcome was associated with the absence of lung metastases ($p=0.007$) or atypical metastatic

sites (spleen, ovarian, bone, breast, adrenal or duodenal; p=0.032), better performance status (ECOG PS < 1; p=0.013) and the presence of a KRAS mutation (p=0.007). In contrast, higher blood CEA levels and neutrophile-to-lymphocyte ratio (NLR) were associated with an increased risk of death (p=0.004 and 0.027, respectively).
Conclusions: Progression of disease in patients with MSI-H/dMMR mCRC treated with ICI rarely occurs in patients experiencing disease control for at least 12 months. Performance status, metastatic pattern, molecular tumor profile, blood CEA levels and NLR can be helpful to identify those patients that may benefit from ICI treatment, guiding clinicians in therapeutic decisions.

- O15 -

IMPLEMENTING ROBOTIC PANCREATIC SURGERY IN BELGIUM, INITIAL 2-YEAR EXPERIENCE IN A HIGH-VOLUME CENTER. V. Hartman (1), B. Bracke (1), T. Chapelle (1), B. Hendrikx (1), D. Ysebaert (1), G. Roeyen (1) / [1] Antwerp University Hospital, Edegem, Belgium, HPB, Endocriene en Transplantatieheelkunde.

Introduction: Laparoscopic pancreatic surgery was introduced in the late nineties. However, laparoscopic pancreaticoduodenectomy (PD) remains a challenging technique which only a few highly skilled surgeons perform. Robotic surgery provides a 3-dimensional stereoscopic and stable view of the surgical field with better dexterity due to its endo-wristed instruments allowing the surgeon to perform complex dissection and precise and accurate anastomoses. In 2001 Giulianotti performed the first robotic PD, followed by the first robotic distal pancreatectomy (DP) by Melvin in 2003.
Aim: In March 2020, the first robotic pancreatic surgery was performed in Antwerp University Hospital following an extensive training program (hands-on course, virtual training on Intuitive Xi robot, training on pig model at ORSI, case observation). We would like to present the results of the first two years of our experience with robotic pancreatic surgery.
Methods: All procedures were performed by two surgeons who alternate between console and patient-side, using the DaVinci XI platform (Intuitive Surgical Inc.). All case-related data were prospectively collected. Complications were scored using the 2016 ISGPS definition. Standardized surgical procedure is to place the patient on a Pink Pad® in Y-position with 15° Trendelenburg, left arm fixed close to the body. With 5° left tilt for PD. Pneumoperitoneum (12mmHg) is created via Verres needle at Palmer's point. Four 8mm robot trocars are placed just above the umbilicus on a horizontal line, 8mm apart. A 12mm assistant trocar is placed under the umbilicus. For PD an additional 5mm trocar is placed 8cm to the right. In DP the parenchymal transection is done with a 60mm Sureform® stapler. To extract the specimen, the infra-umbilical incision is widened to 10-15cm. For PD an Alexis wound protector® is placed to continue with the reconstruction phase. Pancreaticojejunostomy is done with interrupted vicryl 3/0 sutures and a silicon stent is placed in the pancreatic duct. Hepaticojejunostomy is performed with continuous PDS 5/0 in a widened hepatic duct or interrupted PDS 5/0 or 6/0 in a normal hepatic duct. The gastroenterostomy is done side-to-side continuous monolayer V-loc 3/0.
Results: Between March 2020 and March 2022, 64 robotic pancreatic resections were performed. Two patients underwent a total pancreatectomy, and two a central pancreatectomy. Thirty-three patients underwent a full robotic distal pancreatectomy. The spleen was preserved in six patients (19.4%). The main indication was adenocarcinoma (61,3%). The median duration of surgery was 256min [162-468] with median blood loss 200mL. R0 resection was found in 74,2% of cases, indirect R1 in 9,7%, with a median retrieval of 18 lymph nodes. The median hospital stay was 10 days [5-56], with a 30-day readmission of 9,7%. Robotic PD was done in 29 cases. Twenty-two patients had a full robotic procedure. In three patients the pancreaticojejunostomy was remade through a small laparotomy because of a fragile pancreatic remnant. In two patients conversion was due to unexpected tumour contact with the portal vein. One patient was converted because of severe pancreatitis after stenting. Only one urgent conversion for haemorrhage was needed. Median duration of surgery was 468.5min [260-668] with median blood loss 300mL. R0 resection was seen in 19 patients, indirect R1 in 1 patient and true R1 in 4 patients, with a median lymph node retrieval of 18. The median hospital stay was 19 days [8-155], with a 30-day readmission of 24.1%. Postoperative complications are summarized below for both types of surgery. Clavien ≥ 3 POPF grade B or C PPH Chyle leak Bile leak DGE DP 6 (19.4%) 1 (3,2%) 3 (9,7%) 3 (9,7%) N/A 1 (3,2%) PD 12 (41,4%) 3 (10,3%) 6 (20,7%) 4 (13,8%) 0 16 (55,2%)
Conclusions: Both robotic DP and PD are feasible in a high-volume centre with good short-term outcomes, even during the initial learning curve. Further RCT trials are needed to evaluate outcome parameters comparing open, laparoscopic and robotic pancreatic surgery. The overall cost of the procedure is also an important factor to consider. We believe robotic pancreatic surgery will become and remain an important tool in the field of pancreatic surgery.

- O16 -

DECIPHERING THE METHYLOME OF NEUROENDOCRINE TUMORS. L. Mariën* (1), J. Ibrahim* (1), T. Cremers (2), W. Lybaert (3), H. Prenen (4), M. Peeters (5), T. Vandamme (5), G. Van Camp (1), K. Op de Beeck (1) / [1] University of Antwerp, Antwerp, Belgium, Center of Medical Genetics and Center for Oncological Research , [2] University of Antwerp, Antwerp, Belgium, Center of Medical Genetics, [3] Vitaz, Sint-Niklaas, Belgium, Department

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Introduction: The methylome holds great promise for biomarker discovery in neuroendocrine tumors (NETs), as changes in DNA methylation allow differentiation into clinically relevant subgroups and reveal tissue of origin. However, a comprehensive characterization of the NET methylome is lacking, hampering biological insight and meaningful biomarker selection.
Aim: The aim of this study was to investigate the NET methylome through a differential methylation meta-analysis including site-specific controls and other tumor types.
Methods: Our own and public methylation array data (Illumina's Infinium HumanMethylation450 BeadChip) were combined including 60 pancreatic (PNET), 46 small intestine (SINET) and 18 lung NETs (LNET). Beta values were derived from the raw data, normalized using the Beta-Mixture Quantile function and underperforming probes were filtered. Based on the beta values, a differential methylation analysis was performed via a modified linear mixed regression model using the ChAMP package in R. For each type of NET, three subanalyses were run: NET vs. healthy tissue (n=753), NET vs. blood (n=815) and NET vs. 14 other tumor types (n=5786). By taking the intersection of the differentially methylated probes (DMPs) identified in each of the three subanalyses, the PNET-, SINET- and LNET-specific DMPs were identified and used as input for gene set enrichment analysis (GSEA) with methylGSA.
Results: A total of 158.242, 133.236 and 146.721 DMPs were found for PNETs, SINETs and LNETs, respectively of which 69.936 overlapped. GSEA revealed that 1 KEGG and 15 Reactome pathways were significantly enriched for all types including MAPK-related, Akt and Wnt signaling. Moreover, 112 GO categories were shared, yet differences could also be observed between types. In PNETs metabolic processes emerged, whereas in SINETs and LNETs cell cycle regulatory and protein-related categories appeared, respectively.
Conclusions: We provide a comprehensive characterization of the NET methylome, revealing both general and type-specific DMPs and pathways that could serve as a rich source of clinically relevant biomarkers.

- O17 -

RADIOEMBOLIZATION USING HOLMIUM-166 IN PATIENTS WITH UNRESECTABLE HEPATOCELLULAR CARCINOMA: PROSPECTIVE, OPEN LABEL, SINGLE-CENTER PILOT STUDY.

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Introduction: Hepatocellular carcinoma (HCC) accounts for 90% of primary liver cancers and represents a growing health problem worldwide. Recent data demonstrated that personalized dosimetry-based selective internal radiotherapy (SIRT) is associated with better outcome for unresectable HCC. The use of a new isotope, Holmium-166 (166Ho), could offer a more individualized approach in terms of imaging and dosimetry. Current data in the treatment of HCC propose a maximum dose administered to the tumor of 60 Gy, however one recent study by Bastiaannet et al. advocated a minimal absorbed dose of 168 Gy in order to achieve a complete response.
Aim: to evaluate the feasibility and safety of SIRT using 166Ho in a selected population of HCC patients.
Methods: This is an open-label, prospective, non-randomized, single-center pilot study, that included patients with unresectable hepatocellular carcinoma that received 166Ho-SIRT if the work-up using 166Ho scout showed an activity delivered to the tumour ≥ 150 Gy, a less than 60 Gy liver absorbed dose and less than 30 Gy lung shunt fraction. Primary endpoints were feasibility of 166Ho SIRT with this higher dose in our patient population, as well as the assessment of early (24-48h) and late (1 month) safety and toxicity profiles (CTCAE v5.0). Overall response rates (ORR) at 3 months (mRECIST and metabolic response by FDG and choline PET CT) and time to progression (TTP) represented the secondary endpoints.
Results: Between July 2020 and June 2022, 20 patients were included and 15 were treated for a total of 17 treatments (2 patients received 2 treatments). Most patients were men (93.3%) with an underlying compensated (CHILD A) cirrhosis (60%). Mean diameter of lesions was 54±28.7 mm and a median number of 1 lesion. All the attempted treatments were accomplished, despite a difference between the predictive and administered dosage in 7 patients (8 treatments; 26% to 70% difference). Mean administered dose was 175,9 Gy (SD 69,73 Gy), with a mean dose to the non-tumoral liver of 34,86 Gy (SD 20,09 Gy). The mean follow-up time was of almost 10 months. Only grade 1-2 clinical and biological AEs were observed. There were no liver decompensations. At three months 43% and 50% of target lesions showed complete or partial response according to mRECIST. Moreover, 67% and 8% of patients presented a complete or partial response on metabolic assessment. Mean time to progression was of 6 months, however the follow-up is still ongoing.
Conclusions: 166Ho-SIRT using an activity delivered to the tumor ≥ 150 Gy was feasible and safe for patients presenting unresectable HCC. Moreover, response rates are favorable for large tumors with acceptable toxicity profiles and no hepatic decompensation. These findings support further evaluation in larger cohorts exploring response and dosimetry in order to evaluate the benefit of this new isotope and improve the correlation between the predictive and administered dosage.

BELGIAN PANCREATIC CLUB (BPC)

- P01 -

CHARACTERIZATION OF A NEW FORM OF PANCREATITIS. A. Fages (1), M. Rajput Bhatti (2), R. Helaers (3), A. Loriot (3), Y. Achouri (3), M. Fellmann (3), S. Saunier (4), A. Viau (4), A. Serafin (4), I. Scheers (5), P. Jacquemin (2) / [1] UCL Saint Luc, Brussels, Belgium, De Duve Institute - LPAD , [2] UCL Saint Luc, Brussels, Belgium, De Duve Institute - LPAD, [3] UCL Saint Luc, Brussels, Belgium, De Duve Institute, [4] Institut Imagine, Paris, France, INSERM, [5] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Pediatric Gastroenterology and Hepatology.

Introduction: The causes of chronic pancreatitis in children are partly different from those found in adults and remain incompletely understood. Thus, the presence of genetic mutations predisposing is suspected to be a more frequent cause of pancreatitis in children. In this context, among paediatric patients with signs of pancreatitis (increased lipase >3X upper limit of normal, and/or pancreatic imaging anomalies, and/or endocrine/exocrine pancreatic dysfunction), we identified a category of patients with symptoms typically associated with ciliopathies, namely cholestatic liver disease, renal cysts or cognitive deficit. Ciliopathies form a group of genetic disorders related to an impairment of primary cilium function or structure. This organelle is present at the surface of almost all differentiated eukaryotic cells and plays a major role in the regulation of intracellular signaling pathways implicated in embryogenesis, cell cycle and tissue homeostasis.
Aim: Discovering new pathophysiological mechanisms involved in human pancreatitis development, whether in children or adults, is an important step towards a better understanding of the disease and the development of preventive or disease-slowing therapies. In this work, we therefore aimed to identify mutations in ciliary genes in these patients, and to establish a link between these mutations and the development of pancreatitis.
Methods: Via Whole Exome Sequencing of genomic DNA from 43 paediatric patients with idiopathic chronic pancreatitis, we first identified in three of them a mutation in the ciliary/ciliogenic genes PKHD1, HNF1β, and NPHP3. We then focused on the NPHP3 gene and generated by CRISPR/Cas9 technique two new transgenic mouse models: one replicating the NPHP3 gene mutations present in the corresponding patient (NPHP3mut1/mut2 model), while the other is a conditional inactivation of NPHP3 (NPHP3f/f model). Histological analyses were performed on murine pancreas and the phenotypes observed led us to come back to the patients' side. The pancreas of patients was analysed by magnetic resonance imaging and the organ fat content was determined using the IDEAL-IQ application, which enables volumetric fat-fraction mapping and quantification.
Results: The NPHP3mut1/mut2 mice presented renal cysts characterized by tubular dilatations of the distal part of the nephrons, renal inflammation and fibrosis. In their pancreas, we observe the gradual onset of acinar atrophy and lipomatosis, as well as reduced expression of digestive enzymes. We hypothesized that acinar atrophy and lipomatosis resulted from the loss of pancreatic ductal cell homeostasis. The study of Sox9CreER NPHP3f/f mice showed the development of pancreatic acinar atrophy, lipomatosis, ductal hyperplasia, inflammation, and fibrosis. Phenotypic analysis of these two models allowed us to conclude that loss of function of NPHP3 in pancreatic ductal cells led to inflammation and mild fibrosis associated with significant acinar atrophy and severe lipomatosis. This suggests a new form of pancreatitis in these murine models, characterized by a ciliopathic origin. In order to confirm the presence of pancreatic lipomatosis in patients with HNF1β and NPHP3 mutations, initial MRI analyses were performed and revealed a significant percentage of lipomatosis within the pancreas of these patients.
Conclusions: Deeper analysis of mouse models, in particular to characterize the molecular mechanisms involved in the observed phenotypes, and the recruitment of a larger number of patients and control subjects, should allow us to confirm the existence of this new form of pancreatitis of ciliopathic origin.

- P02 -

THE IMPACT OF A MULTIDISCIPLINARY TEAM APPROACH ON THE MANAGEMENT OF FOCAL PANCREATIC LESIONS: A SINGLE TERTIARY CENTER EXPERIENCE. S. Francisse (1), P. Gkolfakis (1), M. Fernandez Y Viesca (1), L. Mans (1), A. Demols (1), M. Pezzullo (2), P. Loi (3), J. Navez (3), J. Closset (3), M. Bali (4), M. Van Wettere (2), N. D'Haene (5), P. Demetter (6), L. Verset (6), C. Bouchart (7), A. Lemmers (1), M. Delhaye (1), J. Devière (1), J.L. Van Laethem (1), M. Arvanitakis (8) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology, [2] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Radiology, [3] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Digestive Surgery, [4] Institut Jules Bordet, Brussels, Belgium, Radiology, [5] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Pathology, [6] Institut Jules Bordet, Brussels, Belgium, Pathology, [7] Institut Jules Bordet, Brussels, Belgium, Radiotherapy, [8] Erasme Hospital, Brussels, Belgium, Gastroenterology.

Introduction: Multidisciplinary team (MDT) meetings aim to optimize patient management by eliminating errors, decreasing time to treatment initiation, and providing better adherence to guidelines. MDT meetings are also associated with changes in the initial diagnosis.

Aim: The aim of this study was to evaluate the impact of MDT discussions on the management and diagnosis of focal pancreatic lesions in a single tertiary center.
Methods: All patients discussed in our institution's MDT meeting on pancreatic diseases from 1/1/2020 to 31/12/2021 with an initial diagnosis of focal (solid or cystic) pancreatic lesion were included. The impact of MDT discussion on patient management, defined as a modification of the initially proposed therapeutic plan after MDT discussion, as well as the criteria leading to this modification were the primary outcomes. Impact on diagnosis was the secondary outcome.
Results: A total of 522 patients [257 (49.2%) females, 65±13.6 years] were included in the study. Of these, 185 (35.4%) and 337 (64.6%) had an initial diagnosis of cystic or solid lesion, respectively. The most common referral query was regarding the management plan (349/522; 66.9%). Endoscopy was the most often proposed procedure before MDT discussion (109/522; 20.9%). Overall, the MDT discussion led to modification of the management plan in 377/522 patients (72.2%), with a statistically significant difference between cystic and solid lesions [63.2% vs 77.2%; $p<0.001$]. Management modifications were mainly driven by revision of cross-sectional radiological images. Regarding diagnosis, adenocarcinoma was the most common diagnosis before MDT (n=250; 47.9%). MDT discussion led to modification of the diagnosis in 92/522 patients (17.6%), with a significant difference regarding cystic lesions (35.7% vs 7.7%; $p<0.001$).
Conclusions: MDT discussion significantly impacts the management of patients with cystic and solid pancreatic lesions leading to a modification of the initially proposed management in two-thirds of them, mainly due to revision of cross-sectional imaging.

- P03 -

PANCREATIC FAT ASSESSMENT USING AI-AIDED WHOLE PANCREAS SEGMENTATION ON MAGNETIC RESONANCE IMAGING: SLICE-BY-SLICE PROTON DENSITY FAT FRACTION IS WIDELY VARIABLE AND IS NOT REPRESENTATIVE OF WHOLE PANCREAS FAT. L. Janssens (1), H. Takahashi (2), H. Nagayama (2), F. Nugen (2), W. Bamlet (3), A. Oberg (3), E. Fuemmeler (2), A. Goenka (2), B. Erickson (2), N. Takahashi (2), S. Majumder (1) / [1] Mayo Clinic, Rochester, United States, Gastroenterology, [2] Mayo Clinic, Rochester, United States, Radiology, [3] Mayo Clinic, Rochester, United States, Quantitative Health Sciences.

Introduction: Excess intrapancreatic fat (IPF) has been implicated as a risk factor for both benign and malignant pancreatic diseases. On magnetic resonance imaging (MRI), IPF can be objectively quantified as proton-density fat fraction (PDFF) using the Iterative Decomposition with Echo Symmetry and Least Squares Estimation (IDEAL) sequence. IPF is known to be heterogeneous, and the widely used approach of using small 2D regions of interest (ROI) in different areas of the pancreas to estimate IPF is likely prone to sampling error and poor interobserver reproducibility.
Aim: Using AI-assisted pancreas segmentation, we aimed to assess the patient-level variability in pancreatic PDFF comparing individual 2D-axial slice to 3D-whole pancreas measurements.
Methods: A total of 245 unique MRI examinations with IDEAL sequences between 1/1/2015 and 6/1/2020 were selected for this study. Of these, 217 MRIs were suitable for whole organ segmentation, 28 were excluded due to artifacts. Pancreas segmentations were performed by annotating the pancreas margin on each axial slice. Segmentation was expedited by an iteratively trained convolutional neural network (CNN). The CNN utilized a UNet architecture with an encoder from the EfficientNet family and was iteratively trained on manually annotated segmentations. All segmentations were manually corrected after CNN-aided annotation. 2D-axial slice pancreas PDFF was derived from all voxels within each axial slice; 3D-whole pancreas PDFF was calculated as the weighted mean of all the 2D-axial slice PDFF values per subject. Intra-individual 2D-axial slice-by-slice pancreas PDFF standard deviation was calculated. Coefficients of variation to assess 2D-axial pancreas PDFF variability were calculated for all segmentations. Boxplots which plotted all 2D-axial slice PDFFs per subject were generated to visualize slice-by-slice variability.
Results: Mean age of our study population was 59.2 years (range 19-89) and 45.6% were female. The mean 3D-whole pancreas PDFF was 23.2% (range 2.0%-79.7%). Intra-individual 2D-axial slice-by-slice pancreas PDFF was widely variable with a mean coefficient of variation of 38.0% (range 2.5% - 97.5%) and individual 2D-axial pancreas PDFFs were not representative of 3D-whole pancreas PDFF (Figure 1 and 2). The 2D-axial pancreas PDFF variability increased with increasing 3D-whole pancreas PDFF (Spearman correlation coefficient 0.51, $p<0.0001$).
Conclusions: 2D-axial pancreas PDFF is widely variable across slices within the same patient and this variability increases with increasing 3D-whole pancreas PDFF. The results of our study indicate that measurement of IPF using 2D ROIs has significant limitations and underscores the need for whole-organ PDFF assessment to objectively and accurately quantify pancreatic fat.

- P04 -

FULL ROBOTIC TOTAL PANCREATECTOMY WITH ISLET AUTOTRANSPLANTATION IN A 18-YEAR-OLD PATIENT. G. Roeyen (1), T. Steinhauser (2), W. Kwanten (2), D. De Paep (3), B. Keymeulen (3), C. De Block (4), T. Jardinet (5), B. Bracke (1), T. Chapelle (1), D. Ysebaert (1), V. Hartman (1) / [1] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Hepatobiliary, Endocrine and Transplantation Surgery, [2] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology and Hepatology, [3] Vrije Universiteit Brussel (VUB), Jette,

Belgium, Beta cell bank - Diabetes Research Center, [4] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Endocrinology - Diabetology, [5] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Radiology.

Case Report: We want to present an 18-year-old female with a hereditary chronic pancreatitis who underwent a full robotic total pancreatectomy with islet autotransplantation (TPIAT). This young patient is known with a hereditary chronic pancreatitis (SPINK 1N34S), treated for years with ductal stenting. She underwent a longitudinal pancreaticojejunostomy in 2016. However, since November 2021 she has been nearly continuously hospitalized because of recurrent attacks of acute upon chronic pancreatitis, leading to a fear of eating with the need for nasojejunal tube feeding and chronic pain treatment with paracetamol, tramadol, bupronorfin, gabapentin and splanchnic block, with only partial pain relief. Preoperative glycaemic testing by means of oral glucose tolerance test showed a normal glucose status. Exocrine testing revealed an already failing digestive function: 6 hours cumulative percentage of the mixed triglyceride breath test was 26% (normal > 23%). BMI was 17.4 kg/m². Izbicky Pain Score was 81. The patient wasn't able to attend school because of continuous hospitalization. A psychologic evaluation was also performed. Because of the small duct nature of this chronic pancreatitis, all other therapeutic options were exhausted. Additionally, because of the already deteriorating exocrine function with preserved endocrine function, the option of TPIAT was considered. In august 2022, a full robotic total pancreatectomy was performed. The pancreas was procured -- including the duodenum but preserving the spleen. Similar to a donor procedure, vascularization was preserved until just before pancreatectomy. Through an enlarged incision, in the scar of the previous pancreatic surgery, the organ could be exteriorized and was perfused with 1 liter of organ preservation solution, and afterwards stored on ice in the same way as a donor organ. This organ was processed in the islet isolation unit of UZ Brussel. The added value of the use of a Da Vinci robot lies in a quicker postoperative recovery because of the minimal invasive technique, and this in combination with a high precision suturing the hepaticojejunostomy (separate 6/0 stitches). For this young woman the smaller incisions (8mm) were of important esthetic value. The day after the procedure, the islet suspension was injected in the liver via the portal vein by the interventional radiologist. The yield was estimated at 1.8x106 beta-cells / kg recipient body weight or 1250 IEQ / kg recipient body weight. Further postoperative recovery was uneventful. Restarting normal oral nutrition took some time because of the long period of tube feeding before surgery. Pancreatic enzyme replacement therapy (PERT) was started. In order to maximize the potential future benefits of this beta cell graft, insulin pump therapy was started immediately postoperatively aiming at glucose levels between 70-120 mg/dl. Postoperative results at 3 months are satisfying. Her endocrine function is recuperating with a C-peptide of 0.5 nmol/l (normal values 0.37-1.47) for a blood glycaemia of 129 mg/dl. Her HbA1c was 5.7%. She gained some weight after increasing the oral intake in combination with PERT, BMI is now 20 kg/m². Her pain medication has been stopped completely, with a decrease in Izbicky Pain score (currently 25). She has also started her university education.

- P05 -

ATYPICAL PRESENTATION OF INFANTILE EXOCRINE PANCREATIC INSUFFICIENCY DUE TO SPINK1 GENE MUTATION DETECTED BY RAPID WHOLE GENOME SEQUENCING STUDY IN A 5-YEAR-OLD BOY.
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Introduction: Infantile exocrine pancreatic insufficiency (EPI) is a rare condition, most frequently encountered as part of cystic fibrosis. Infantile isolated EPI and Serine protease inhibitor Kazal type 1 (SPINK1) gene mutations have been reported for the first time in two infants by Venet et al. Here, we report the third paediatric case of isolated IPE related to SPINK1 mutation, initially presenting hepatic failure features.
Case report: A 5-year-old boy was referred to our paediatric department for abnormal laboratory test results. He was born at term with a low weight (2490 g, -1.87 Z-score). Failure to thrive was noticed since he was 4 months old. Parents reported that he consistently had loose fatty stools. He also had persistent conjunctivitis. Family history revealed consanguinity and several individuals with hepatic and pancreatic disorders, including sclerosing cholangitis in his father and recurrent pancreatitis in his mother and maternal uncle. Physical examination showed oedema, bloated abdomen, hepatomegaly and facial dysmorphism including broad and high forehead, bushy eyebrows, small nose, thin upper lip and low-set ears. Laboratory findings revealed signs of hepatic failure and intestinal malabsorption with hypoalbuminemia, severe fat-soluble vitamin deficiencies, coagulation disorder and hyperammonemia. Hepatic enzymes and bilirubin were subnormal. Abdominal ultrasound and cholangio-MRI revealed hepatosplenomegaly with normal appearance of the bile ducts. Oesogastroduodenoscopy showed oesophagitis and gastritis with focal villous hypotrophy on duodenal biopsies. Colonoscopy was normal. Hepatic biopsy demonstrated steatosis and fibrosis (F2-Metavir). Fibrosing sclerosing conjunctivitis was noticed in ophthalmologic evaluation and MRI identified optic nerve atrophy.

Extensive metabolic, infectious and autoimmune investigations returned normal. The acid steatocrit value was normal and steatorrhea analysis could not be interpreted. No clinical, biological or radiological sign of pancreatitis was found. The patient was included in rapid whole genome sequencing (rWGS) study, which identified a frameshift homozygous loss-of-function mutation in SPINK1 gene (NM_003122.3:c.27delC; p.Ser10fs), located on the first exon. This deletion was present in both parents in a heterozygous state. Subsequently, faecal elastase-1 (FE-1) concentration was tested and was significantly reduced (4µg/g, N>200 µg/g). Diagnosis of infantile isolated EPI related to SPINK1 mutation was made based on intestinal malabsorption features, genetic results and FE-1 level. With regards to the signs of hepatic failure, we assumed these are secondary and due to severe malabsorption and malnutrition. Likewise, conjunctivitis and optic nerve atrophy were likely the result of severe vitamin A deficiency. Pancreatic enzyme replacement therapy was started and led to stools normalisation, weight gain and improvement in liver function.
Discussion: SPINK1 gene encodes a trypsin inhibitor protein which has been considered to prevent premature activation of digestive enzymes by trypsin in pancreatic tissue. Heterozygous pathogenic SPINK1 mutations exert a predisposing effect for hereditary pancreatitis (HP) and are considered disease-modifying mutations. The specific c.27delC mutations, inherited in a heterozygous or homozygous form, have been described in at least ten patients with HP with variable phenotypic expressivity. In 2017, Venet et al. reported for the first time two homozygous loss-of-function SPINK1 mutations associated with isolated infantile EPI. The two infants presented intestinal malabsorption signs. One of them showed cytolytic and cholestatic liver damage without hepatic insufficiency. EPI is characterised by steatorrhea and malabsorption disorders such as nutritional deficiencies, particularly of fat-soluble vitamins, and poor growth. The homozygous c.27delC mutation supposes a pathogenic role, leading to diagnosis of infantile isolated EPI related to SPINK1 mutation. This diagnosis is even more strengthened as the FE-1 level is very low. Southern blot to detect large deletion for Pearson's syndrome is currently in process, as well as the sweat test to exclude a cystic fibrosis. Interestingly, the clinical presentation was atypical and mainly suggestive of liver failure. This indicates that EPI should be considered in the assessment of unexplained liver failure.
Conclusion: We report an atypical case of severe infantile isolated EPI, due to SPINK1 mutation. Our diagnosis is based on SPINK1 frameshift homozygous mutation (c.27delC) detected by rWGS, low faecal elastase level, signs of intestinal malabsorption and response to pancreatic enzyme replacement therapy. In this case, initial features of hepatic failure were probably due to severe and chronic malabsorption and malnutrition.

- P06 -

MASK OFF: A DECEPTIVE CASE OF PANCREATIC MASS K. Sarti (1), I. Borbath (1), D. Hoton (2), P. D'Abadie (3), L. Coubeau (4), P. Deprez (5) / [1] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Hepato-gastroenterology and digestive oncology, [2] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Pathology, [3] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Nuclear medicine, [4] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Abdominal transplant and hepatobiliary surgery, [5] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Hepato-gastroenterology.

Case Report: We describe the case of a 74-year-old man who underwent a liver transplantation in 2006 in the setting of hepatocarcinoma resulting from alcohol induced cirrhosis. Since 2016, the patient was found to have a steadily rise in alpha-fetoprotein (AFP) levels prompting repeated multimodal imaging, with no diagnostic yield; the patient was asymptomatic. In 2022, cholangio-MRI revealed a 3 cm mass located in the posterior segment of the pancreatic head and enlarged inter-aorto caval lymph nodes. Bloodwork showed normal CA19.9 and elevated AFP (>300 µg/L). Endosonography (EUS) was then performed, describing a hypervascularized pancreatic lesion. EUS-acquired tissue samples were non-contributive. Given the hyperarterialized characteristic of the mass, patient underwent 68Ga-DOTA-TATE, demonstrating increased uptake in the pancreatic lesion as well as in inter-aorto caval lymph nodes. A second EUS with fine needle biopsy (FNB) of the pancreatic mass was then performed. Histopathology and immunohistochemical profile were compatible with hepatocellular carcinoma (HCC). Given the somatostatin imaging positivity of both pancreatic mass and lymph nodes, the patient was started on long-acting somatostatin analogs (somatuline Autogel120 mg administered every 28 days). Somatostatin receptors (SSTRs) expression in HCC cells is uncommon but described. The use of SSA has been studied in a few randomized control trials with conflicting results. Pancreatic metastases of HCC are rare, with but a few cases described in the literature. To our knowledge, this is the first case of a pancreatic metastasis as the initial presentation of an HCC recurrence 16 years after liver transplant and exhibiting SSTRs expression.

- P07 -

A PANCREATIC ARTERIOVENOUS MALFORMATION CAUSING ANGOR ABDOMINALIS. J. Goos (1), F. Kastelein (1), W. Lammers (1), P. Van Doormaal (2), L. Oudijk (3), R. De Wilde (4), L. Van Driel (1), M. Bruno (1), W. Kwanten (5) / [1] Erasmus MC, University Medical Center Rotterdam, The Netherlands, Department of Gastroenterology and Hepatology, [2] Erasmus MC, University Medical Center Rotterdam, The Netherlands, Department of Radiology and Nuclear Medicine, [3] Erasmus MC, University Medical Center Rotterdam, The Netherlands, Department of Pathology, [4] Erasmus MC, University Medical Center Rotterdam, The Netherlands, Department of

Surgery, [5] Universiteit Antwerpen / Antwerp University Hospital, WILRIJK (Antwerpen), Belgium, Department of Gastroenterology and Hepatology.

Case Report: A 53-year-old male presented in our outpatient clinic with severe epigastric pain that intensified postprandially. These symptoms were present for three months with increasing intensity and frequency over time. Furthermore, one episode of melaena was observed. Additional assessments showed normal blood work and gastroscopy. Abdominal CT angiography revealed an arteriovenous malformation (AVM) with a maximum diameter of 55 mm located in the pancreatic head arising from both the superior mesenteric artery (three branches) and hepatic artery (two branches) with venous drainage in the superior mesenteric vein. As pancreatitis and other causes of abdominal pain were excluded, the abdominal pain was attributed to a pancreatic steal syndrome caused by the AVM. Subsequent digital substraction angiography confirmed the diagnosis. However, endovascular embolization was deemed impossible because of the diffuse nidus engulfing the complete pancreatic head and the absence of a target vein suitable for a transvenous approach. After multidisciplinary team meeting, therefore, a pancreatoduodenectomy with Roux-en-Y gastrojejunal anastomosis was proposed and performed. Pathological examination reconfirmed the diagnosis. The hospital stay was complicated by a grade B pancreatic fistula. The patient was discharged home twelve days postoperatively. During the postoperative course, the pain that was present pre-operatively subsided rapidly and analgesics were discontinued after a month. A CT scan was performed two months postoperatively, showing a postoperative anatomy without signs of any arteriovenous malformation. The subsequent follow-up time comprising 6 months was uneventful. Endocrine insufficiency occurred with the need of long-acting insulin and metformin. The exocrine function was also compromised with a clinically mild steatorrhea at the last visit despite of the use of a pancreatic enzyme supplement (dose was subsequently increased). Pancreatic AVMs are rare anomalies of the pancreatic vasculature, that can be congenital or acquired. Congenital AVMs are either isolated or seen in association with Rendu-Osler-Weber disease. Acquired cases (arteriovenous fistula) are seen after trauma, surgery or infection. Pancreatic AVMs are most prevalent in male patients (85% of the cases), and mostly located in the pancreatic head (59%). While patients are generally asymptomatic, some develop typical symptoms of gastrointestinal bleeding and abdominal pain. Abdominal pain can be caused by portal hypertension which was not present in our case, or by a steal phenomenon, in which the blood shunts away from the mesenteric circulation through the AVM. In conclusion, angor abdominalis can be caused by pancreatic AVMs. In case local treatment is not an option, surgery is a justifiable alternative treatment.

BELGIAN WORKING GROUP OF DIGESTIVE PATHOLOGY

- R01 -

PRIMARY EXTRARENAL RHABDOID TUMOUR OF THE LIVER: A CASE REPORT AND LITERATURE REVIEW. M. Meyers (1), P. Demetter (2), A. De Roo (3), M. Pezzullo (4), B. Brichard (5), C. de Magnée (6), R. De Krijger (7), G. Verset (8) / [1] Hopital Erasme, ULB, Belgium, Gastroenterology, [2] Institut Jules Bordet, Brussels, Belgium, Pathology, [3] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Pathology, [4] Hopital Erasme, ULB, Belgium, Radiology, [5] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Paediatric Haematology and Oncology, [6] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Paediatric Digestive Surgery, [7] University Medical Center Utrecht, The Netherlands, Pathology, [8] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology.

Case Report:

Background: Extrarenal rhabdoid tumours (ERT) are highly aggressive tumours that are poorly responsive to standard cytotoxic chemotherapy and are associated with a grim prognosis. Primary ERT of the liver are most commonly seen in early childhood and exceptionally rare later in life.
Case presentation: We report the case of a 16-year-old otherwise healthy male patient, presenting with flu-like symptoms, after his second COVID-vaccination. During the work-up, a large solid liver lesion was incidentally discovered upon abdominal ultrasound examination. Anatomopathological work-up rendered the diagnosis of primary ERT of the liver, characterised by loss of expression of INI-1 protein, encoded by the SMARCB1 gene. We discuss and summarize the existing literature by reviewing 53 paediatric and 6 adult cases as well as treatment, outcome, and histopathological features of primary hepatic ERT.
Conclusion: Primary ERT of the liver is usually not associated with specific signs or symptoms, making the diagnosis very challenging. As ERT are associated with a high metastatic rate, delayed diagnosis leads to increased mortality as complete resection is not feasible in advanced stage cases. Therefore, early diagnosis enabling complete resection of the tumour is crucial to improve patient outcome. Of interest, primary ERT of the liver are associated with biallelic loss of the SMARCB1 gene, a potential target for cancer therapeutics. This is the first case to our knowledge of hepatic rhabdoid tumour treated with liver transplantation.

- R02 -

THE CHALLENGING DIAGNOSIS OF T CELL INFILTRATION IN THE LIVER IN POST-TRANSPLANTED PATIENT. A. Camboni (1), X. Stephenne (2), M. De Ville de Goyet (3), P. Baldin (4) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Department of Pathology, [2] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Pediatric Gastroenterology, [3] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Pediatric Hematology and Oncology, [4] Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium, Pathology.

Introduction: Post-transplant lymphoproliferative disorders (PTLDs) represent a severe complication after solid organ transplantation. The majority of PTLDs are of B-cell origin and are associated with Epstein–Barr virus (EBV) infection. T-cell PTLDs are significantly rarer and infrequently associated with EBV.
Aim: We report a case of T-cell PTLD in 2-year-old girl underwent liver transplantation due to biliary atresia and discuss the histopathological differential diagnosis in liver biopsy.
Methods: One year after the transplantation, liver test was increased. A rejection was clinically suspected, and liver biopsy revealed a discrete atypical lymphocytic infiltrate in the portal tracts and parenchyma showing a T-cell receptor rearrangement. Immunohistochemically, lymphocytes were mostly of T-lineage CD3+/CD5+/CD2+/, showed a cytotoxic phenotype (CD8+/ TiA1+/Granzyme+/Perforin+/) and no expression of T-cell receptor beta F1. Epstein-Barr encoding region (EBER) in situ hybridization was negative.
Results: These aspects were compatible with monomorphic T-cell PTLD, EBV negative, showing overlapping features between an hepatosplenic T-cell lymphoma (HSTCL) and a T-large granular lymphocytic (T-LGL) leukaemia. These two entities differ enormously in prognosis and consequent in treatment, as HSTCL shows an aggressive clinical course and T-LGL is quite indolent. To try to differentiate the 2 diseases, fluorescence in situ hybridization for i(7q) was performed and results were negative reassuring for a diagnosis of T-LGL leukaemia. However negative finding of i(7q) does not necessarily exclude HSTCL because not all HSTCLs have i(7q). A PET-CT was performed, and no spleen or bone marrow involvement were detected. All these data suggested a diagnosis of γδ T-LGL leukaemia and Rituximab treatment was initiated. Three months later, the patient showed good clinical condition confirming the indolent clinical behaviour of the disease.
Conclusions: Integration of morphologic assessment and comprehensive immunophenotyping with the clinical features and genetic results is critical to the correct classification of these rare and complex lesions. Finally, multidisciplinary meeting is recommended to complete the diagnosis.

- R03 -

A BOY AT TERM WITH AN UNUSUAL MASS IN THE THORAX. B. Verbraeken (1), A. Driessen (1) / [1] University hospital of Antwerp, Edegem, Belgium, Pathology.

Case Report: Our case was a male neonate, who was delivered on term with an emergency caesarean, which had to be performed due to foetal distress. The child had to be intubated and was directly transferred to the paediatric intensive care unit. Prenatal imaging had already revealed a mass in the right hemithorax. Postnatal radiological examination showed an associated malrotation of the intestine. A diagnosis of a bronchopulmonal foregut malformation was initially proposed, but this was unlikely because of the discovery of associated vertebral anomalies. The development of a necrotising enterocolitis necessitated surgical intervention about three weeks postpartum. During surgery, a part of the jejunum showed to be involved by NEC. Besides this necrotising enterocolitis a diverticulum was diagnosed. This diverticulum formed the aforementioned mass in the thorax. The entire process was resected without complications. Anatomopathological examination revealed a gastric ectopia, in the diverticle. Moreover, in association with this gastric ectopia a mature teratoma was found in the top of this diverticle. Despite successful surgery and appropriate postoperative management, the patient died at the age of four months due to respiratory distress syndrome. Our boy has an uncommon congenital disorder, consisting of a combination of enteric and vertebral anomalies. This congenital disorder is the split notochord syndrome, described by Bentley and Smith in 1960. It is believed to be caused by an abnormal splitting of the notochord. The notochord is a cellular rod, which develops by transformation of the notochordal process during the third week of human development. Besides its role in the development of the axial skeleton, it is also involved in the differentiation of the endoderm of the gut. The split notochord syndrome encompasses a range of congenital malformations, including enteric or mediastinal cysts, combined with vertebral or spinal cord abnormalities. Enteric duplications and diverticula have also been described. The combination of a split notochord syndrome and a mature teratoma is an extremely uncommon finding.

- R04 -

COLLAGENOUS GASTRITIS: A RARE CAUSE OF IRON DEFICIENCY ANEMIA IN A 6-YEAR-OLD BOY. L. Delmotte (1), E. Makridi (1), L. Verset (2), L. Kornreich (3), K. Kotilea (1), P. Bontems (1) / [1] Queen Fabiola Children's University Hospital, Brussels, Belgium, Clinic of Paediatric Gastroenterology, [2] Institut Jules Bordet, Brussels, Belgium, Pathology, [3] Queen Fabiola Children's University Hospital, Brussels, Belgium, Clinic of Hematology-Oncology.

Introduction: Clinical, endoscopic, and histopathologic features of collagenous gastritis illustrated by a case report presenting with severe anaemia.
Aim: Description of case and review of literature.
Methods: A 6-year-old boy was admitted in our hospital presenting paleness, extreme fatigue, and intermittent epigastric pain. Initial investigations revealed severe microcytic hypochromic regenerative anaemia (haemoglobin was 4,5 g/dl) and a severe iron deficiency. A faecal occult blood test was positive. He was transfused with packed red blood cells and was given intravenous iron. Workup for anaemia revealed no intraerythrocytic enzymes deficit, no anomaly in erythrocyte membranes nor hemoglobinopathies. No parasitic infection or lead intoxication was detected. Upper gastrointestinal endoscopy was performed.
Results: Endoscopy showed hypertrophic and nodular mucosa in the gastric body with presence of coagulated blood. The antral mucosa was not affected. The histopathologic findings of the fundus biopsies revealed severe progressive chronic gastritis with abrasion of the epithelium, thickening of the collagen plate and lymphocytic infiltrate in the lamina propria compatible with collagenous gastritis. H. pylori infection was excluded. After failure of first line treatment with proton-pump-inhibitors (PPIs), systemic corticosteroids were prescribed. After one month of treatment, he presented at the follow-up with improved clinical and endoscopic images. However, histopathologic findings of biopsies persisted.
Conclusions: Collagenous gastritis is a rare condition in children. Only a few case series have been published. The role of the pathologist is crucial as the symptoms overlap with other GI conditions (anaemia, GI bleeding, abdominal pain) and endoscopic image might be suggestive but not specific. Corticosteroids and PPIs seem to be an efficient treatment. Patients with collagenous gastritis need long-term follow-up and monitoring as the prognosis is still unknown. There is a need for further clinical trials and a better understanding of the pathogenetic mechanisms.

- R05 -

COMMON VARIABLE IMMUNODEFICIENCY DISORDER (CVID) MIMICKING CROHN'S DISEASE: HISTOPATHOLOGICAL CLUES THAT MAY LEAD TO THE CORRECT DIAGNOSIS. L. Velthof (1), J. Geldof (2), J. Van Dorpe (3), T. Lobatón Ortega (2), A. Hoorens (3) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Pathology, [2] Ghent University Hospital, Ghent, Belgium, Gastroenterology, [3] Ghent University Hospital, Ghent, Belgium, Pathology.

Case Report: Common Variable Immunodeficiency Disorder (CVID) can present with heterogeneous clinical manifestations, including recurrent infections, autoimmune diseases, gastrointestinal disorders or malignancies. Gastrointestinal manifestations are common and include acute and chronic infectious diarrhoea and non-infectious enteropathy. The latter occurs in about 10% of CVID patients, and may resemble other gastrointestinal disorders, such as Crohn's disease, ulcerative colitis, celiac disease or microscopic colitis. We present a 61-year-old patient who was initially, at the age of 33, diagnosed with Crohn's disease, and in whom CVID was only discovered 18 years later, after a persistent pneumonia. Review of gastrointestinal biopsies revealed some histopathological features that are rather atypical of Crohn's disease and may indicate CVID. Better awareness of these features may contribute to an earlier diagnosis of CVID and prevent devastating and life-threatening complications.

- R06 -

GRANULOMAS IN THE BOWEL DOES NOT ALWAYS FIT CROHN'S DISEASE. K. De Corte (1), N. Moes (2), A. Driessen (1) / [1] University Hospital Antwerp, Edegem, Belgium, Pathology, [2] University Hospital Antwerp, Edegem, Belgium, Pediatric Gastroenterology.

Case Report: Inflammatory Bowel Disease is comprised of two major disorders: ulcerative colitis and Crohn's disease. Both are chronic and relapsing inflammatory disorders involving different segments of the gastrointestinal tract, varying in extent and severity over time. Their main features include architectural disturbance and basal plasmacytosis. Distinction between the two subtypes can be made based on the distribution of the inflammatory component and on the possible presence of granulomas. Latter can be found in up to 50% of paediatric patients with Crohn's disease, while being less frequent in adults. Still, intestinal inflammation with the presence of granulomas is not necessary diagnostic for Crohn's disease, as demonstrated by our case report.
We present a case of a 10-year-old boy who was referred to a paediatrician following significant weight loss and diarrhoea over a period of 3 months. There was no noteworthy medical or family history. The patient was admitted to the university hospital for diagnostic work-up, which comprised blood analysis, echography, radiology and CT. Based on the clinical presentation and results from these additional tests a diagnosis of Inflammatory Bowel Disease was proposed, followed by a gastroduodenal- and ileocolonoscopy. Biopsies from the terminal ileum showed a diffuse chronic inflammation with numerous granulomas. The unusual appearance of these granulomas provided a differential diagnostic problem, in which an infectious disease was considered. However, an infection could not be proven by clinical tests. In the end, the revelation of additional family history helped to solve this differential diagnostic problem. In conclusion, our case shows that the presence of granulomas is not sufficient for the diagnosis of Crohn's disease. The number, size and appearance of the granulomas gives rise to a broad differential diagnosis, one in which infectious disease is an important consideration.