

ABSTRACTS

38th Belgian Week of Gastroenterology 2026

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

-A01-

HYPOXIC HEPATITIS ... 35 YEARS LATER. E. Kaze (1), V. Huberlant (2), J. Henrion (3) / [1] Cliniques de l'Europe Site Sainte-Elisabeth, Uccle, Belgium, Hépatogastroentérologie, [2] CHU Helora, La Louvière, Belgium, Unité de Soins Intensifs, [3] CHU Helora, La Louvière, Belgium, Médecine Interne, Service d'Hépatogastroentérologie.

Rationale: Hypoxic Hepatitis (HH) is defined by a massive and brutal elevation of serum aminotransferases activities (S-AT > 20XULN) occurring in the context of hemodynamic failure, after exclusion of other causes of acute hepatocellular necrosis. Thirty-five years ago, we collected the first large series of HH (more than 100 cases) and subsequently, we reported the first hemodynamic study on this topic (1). Recently, we had the impression that the clinical profile of HH has changed. **Aim:** The aim of this study was to assess whether the frequency, causes and prognosis of HH have changed over the last 35 years.

Methods: In this study, we compared a series of 138 cases of HH prospectively collected during a 10-year period (1981 to 1991 - Series 1) to a series of 139 cases of HH retrospectively collected during a 4-year period (2020 to 2023 - Series 2). Both series were collected in the intensive care units (ICUs) of the same hospital under the supervision of the same investigator (JH). For Series 1, a new analysis of the individual data – still available – was performed. For Series 2, cases of HH were identified through the hospital laboratory database by screening for all ICU patients with S-AT $\geq$ 20XULN followed by review of their electronic medical records.

Results: There were no significant differences in age and gender between the two series with a 65% male prevalence in both series and a mean age of 68 years in Series 1 compared to 67 years in Series 2. The prevalence of HH in ICUs increased from 0.8% (138/15,616 admissions) in Series 1 to 2.5% (139/5118 admissions) in Series 2 ($p < 0.001$). The main causes of hemodynamic failure were cardiac in 67% versus 45% ($p < 0.001$), respiratory in 17% versus 8% ($p < 0.02$), toxic-infectious in 12% versus 27% ($p < 0.01$) or hypovolemic-haemorrhagic in 1% versus 17% ($p < 0.001$) between Series 1 and Series 2, respectively. The in-hospital mortality was higher in the more recent cohort : 56% in Series 1 versus 68% in Series 2 ($p = 0.05$).

Conclusions: The clinical profile of HH has changed markedly over the last decades. The frequency of HH in ICUs has increased, the underlying causes of hemodynamic failure have evolved and the mortality has not decreased despite advances in intensive care medicine.

Reference: 1/ Henrion J, Schapira M, Luwaert R, Colin L, Delannoy A, Heller F R. Hypoxic hepatitis. Clinical and hemodynamic study in 142 consecutive cases. *Medicine* 2003; 82:392–406.

-A02-

CARDIOMETABOLIC RISK FACTOR BURDEN PREDICTS LONGITUDINAL LIVER STIFFNESS TRAJECTORIES IN MASLD-RELATED cACLD. Z. Gadi (1), L. Schoenmakers (1), W. Kwanten (1), L. Vonghia (1), S. Francque (1) / [1] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology & Hepatology.

Introduction: Cardiometabolic risk factors (CMRFs) related to metabolic dysfunction-associated steatotic liver disease (MASLD) include overweight/obesity, impaired glucose metabolism, arterial hypertension, hypertriglyceridemia and low high-density lipoprotein (HDL) cholesterol. In MASLD-related compensated advanced chronic liver disease (cACLD), the combined impact of CMRF burden on longitudinal liver stiffness behaviour, a non-invasive monitoring tool, remains insufficiently defined.

Aim: To evaluate the association between CMRF burden and longitudinal changes in liver stiffness measurement (LSM) in patients with MASLD-related cACLD.

Methods: We included ninety-three adults with biopsy-proven MASLD and cACLD, defined by histological proven F3-F4 fibrosis. Inclusion required two Vibration-Controlled Transient Elastography (VCTE) measurements $\geq$ 1 year apart with paired biochemical assessment. Exclusion criteria were other causes of liver disease (including alcohol-related liver disease or metALD), previous bariatric surgery, previous or current hepatic decompensation at baseline, and previous liver transplantation. Baseline

CMRFs (range 1-5) were recorded. LSM trajectories were evaluated as absolute and percentage change, and categorised as improved ($\geq 20\%$ decrease), stable (-20% to $+20\%$), or worsened ($\geq 20\%$ increase). Clinical outcomes included incident hepatic decompensation events and all-cause mortality. **Results:** The cohort comprised 55 men (59%) and 38 women (41%), with F3 fibrosis in 62 patients (67%) and F4 in 31 (33%). CMRF burden was high: 1 CMRF in 2 patients (2.2%), 2 in 13 (14.0%), 3 in 32 (34.4%), 4 in 27 (29.0%), and 5 in 19 (20.4%), with 78 patients (84%) having ≥ 3 CMRFs. Baseline LSM increased with metabolic load (17.85 kPa in 1 CMRF; 16.16 kPa in 2; 15.44 kPa in 3; 21.08 kPa in 4; 21.98 kPa in 5 CMRFs). Baseline biochemical markers also worsened with increasing CMRF burden, with higher AST (23 to 58.6 U/L), ALT (38.5 to 85.1 U/L), GGT (40.5 to 149.5 U/L), and triglyceride levels (98 to 251.9 mg/dL), alongside lower HDL concentrations (55.0 to 31.8 mg/dL) in the 4-5 CMRF groups compared to 1-3. Mean longitudinal LSM change varied across CMRF strata: -6.95 kPa (-38.9%) in 1 CMRF, -3.53 kPa (-21.8%) in 2, +3.01 kPa (+19.5%) in 3, -2.41 kPa (-11.4%) in 4, and -0.33 kPa (-1.5%) in 5 CMRFs. Overall, 35 patients (39%) improved, 31 (34%) remained stable, and 24 (27%) worsened, with LSM progression most frequent in the 3-CMRF (35%) and 5-CMRF (44%) groups. During a median follow-up of 4.3 years, 5 patients (5.4%) developed ascites and 5 (5.4%) had non-bleeding oesophageal varices detected on endoscopy. No variceal bleeding, hepatic encephalopathy, hepatocellular carcinoma, or liver transplantation occurred. All-cause mortality occurred in 7 patients (7.5%), of whom 3 had liver-related causes. All patients who died had a high metabolic burden with ≥ 3 CMRFs. Among them, 3 had 3 CMRFs, 2 had 4 CMRFs, and 2 had 5 CMRFs. In the 6/7 individuals with paired VCTE measurements, liver stiffness increased from a mean of 22.2 kPa at baseline to 33.8 kPa at follow-up (mean change +11.6 kPa). Individual trajectories showed substantial variability, with some patients experiencing very marked worsening, up to +36.7 kPa.

Conclusions: In MASLD-related cACLD, CMRF burden strongly influenced longitudinal LSM dynamics. Patients with lower metabolic burden demonstrated the greatest LSM improvement, whereas those with 3 or 5 CMRFs showed the highest likelihood of LSM progression. These findings highlight the role of metabolic drivers in disease activity and progression in MASLD cACLD and support integrating cardiometabolic profiling into routine risk stratification and monitoring.

-A03-

MULTIVISCERAL TRANSPLANTATION IN TWO EUROPEAN CENTRES: INDICATIONS AND OUTCOME. C. Boelhouwer (1), A. Desmedt (2), C. Evers (3), B. Heřmanová (4), D. Kostrouch (5), A. Dubois (6), D. Monbaliu (6), T. Vanuytsel (7), L. Ceulemans (8), J. Fronek (4), J. Pirenne (6) / [1] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Abdominal Transplantation, [2] KU Leuven, Leuven, Belgium, Abdominal Transplantation, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Abdominal Transplantation, [4] Institute of Clinical and Experimental Medicine, Praha, Czech Republic, Abdominal Transplantation, [5] Institute for Clinical and Experimental Medicine, Prague, Czech Republic, Abdominal Transplantation, [6] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Abdominal Transplantation, [7] Translational Research Centre for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Gastroenterology, [8] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Thoracic surgery.

Introduction: Multivisceral transplantation (MVTx, liver/stomach/pancreas/intestine) and modified MVTx (mMVTx, stomach/pancreas/intestine) are life-saving procedures mostly/classically for patients with diffuse splanchnic thrombosis, but increasingly for other complex diffuse abdominal diseases. The procedure is considered high-risk, only few European centres have started MVTx programs (most series originate from the US).

Aim: We aim to report the initial experience (indication/management/outcome) at 2 European centres (sharing similar protocols).

Methods: A retrospective study was conducted, analysing all (m)MVTx performed at 2 European hospitals between 2007 and 2024. 26 procedures (performed on 25 patients) were included, with median (min-max) follow-up of 1.5 (0-10.22) years.

Results: Median (min-max) recipient age was 43 (2-66) years (1 child), 8/26 (31%) female. 23/26 (88%) MVTx and 3/26 (12%) mMVTx. Indications: diffuse splanchnic thrombosis (50%) {of which 54% with associated liver failure}; desmoid tumour (15%); NET tumour (4%); diffuse arterial ischemia (8%); chronic intestinal pseudo-obstruction (4%); re-MVTx due to rejection (4%); and other abdominal catastrophes (19%). Arterial embolization and continuous veno-venous hemofiltration were used in 9/26 (35%) and

15/26 (57%) procedures, respectively. Median ICU/hospital stay: 26 (1-73)/73 (1-197) days; acute rejection (65%); 1-/5-/10-yr patient & graft survival: 67%/60%/48% and 67%/54%/43%, respectively. Causes of death: sepsis (45%); cardiogenic shock (18%); tumour (18%); rupture aortic tube (9%); and suicide (9%).

Conclusions: (m)MVTx is a complex (&underused) life-saving procedure for patients with diffuse abdominal diseases not amenable to other standard (transplant) procedures. Lessons learned from this series and consecutive protocol adjustment over time (patient selection, perioperative medical/surgical strategy, postTx follow-up) have led to improved results in more recent years.

-A04-

UNDER THE RADAR: BARIATRIC SURGERY, ALCOHOL AND LIVER HEALTH IN PSYCHIATRIC CARE. J. Bert (1), S. Lefere (2), W. Verlinden (3), H. Van Vlierberghe (2), X. Verhelst (2), S. Raevens (2), G. Heylens (4), A. Geerts (2), J. Schouten (3), L. Onghena (2) / [1] Ghent University, Ghent, Belgium, Faculty of Medicine and Health Sciences, [2] Ghent University Hospital, Ghent, Belgium, Liver Research Centre Ghent, [3] Vitaz, Sint-Niklaas, Belgium, Department of Hepatology and Gastroenterology, [4] Ghent University Hospital, Ghent, Belgium, Department of Adult Psychiatry.

Introduction: Bariatric surgery (BS) is increasingly performed to treat obesity and its metabolic complications. While it often improves hepatic steatosis, emerging evidence suggests a paradoxical increase in the risk of alcohol use disorder (AUD) and severe alcohol-related liver disease postoperatively.

Aim: This study investigates the impact of prior BS on substance use patterns, AUD severity and liver-related risk factors among patients with excessive alcohol use on a psychiatric ward. This largely overlooked population often prioritizes psychiatric care over physical health follow-up. Through this study, we aim to elucidate the interplay between prior BS, alcohol use and liver health in a high-risk psychiatric cohort.

Methods: This cross-sectional Belgian study enrolled adult patients admitted for excessive alcohol use to the Urgent Psychiatric Care Unit of Ghent University Hospital between May 2023 and December 2023 (n=36) and to the psychiatric department (PD) of AZ Vitaz between October 2024 and November 2025 (n=147). Written informed consent was obtained from all participants. Laboratory results and clinical information were retrieved from electronic medical records and liver assessments with abdominal ultrasound and FibroScan were performed during hospital admission. Patients admitted to the PD also completed self-report questionnaires assessing sociodemographic characteristics, substance use (WHO ASSIST) and the severity of alcohol use disorder (AUDIT). Participants were categorized according to their history of bariatric surgery and associations with clinical outcomes were examined using univariate and multivariate logistic regression analyses.

Results: A total of 183 patients were included in the study. The prevalence of prior BS was 25,7%. Reported procedures included Roux-en-Y gastric bypass (n=30), Roux-en-Y gastric bypass with minimizer (n=7), sleeve gastrectomy (n=6), mini-gastric bypass (n=2), gastric banding (n=1) and Billroth II reconstruction (n=1). In univariate analyses, patients with prior bariatric surgery were more often female ($p<0,001$) and had a higher body mass index (BMI) ($p<0,001$). They also exhibited significantly lower haemoglobin ($p<0,001$), white blood cell count ($p=0,003$), creatinine ($p=0,027$) and alanine aminotransferase ($p=0,037$) levels, along with higher alkaline phosphatase ($p=0,003$) and higher Model for End-Stage Liver Disease (MELD) scores ($p=0,019$) compared with the non-bariatric group. In addition, bariatric patients were more often admitted to the hepatology department following psychiatric hospitalization. Finally, they presented with more advanced liver fibrosis ($p=0,008$), despite steatosis being equally severe. In multivariate analysis, a history of BS remained independently associated with the presence of presumed compensated advanced chronic liver disease (FibroScan ≥ 15 kPa) after adjustment for BMI, gender and self-reported daily alcohol consumption ($p=0,025$; OR 4,05; 95% CI:1,2-13,74). Within the PD subgroup, the duration of AUD was significantly shorter among patients who underwent BS ($p = 0,018$). Regarding substance use disorders, tobacco use was significantly lower following bariatric surgery ($p < 0,001$). On average, AUD developed five years after BS, although 20% of patients already reported excessive alcohol use prior to the procedure.

Conclusions: Among all patients admitted for excessive alcohol use, one quarter had previously undergone bariatric surgery. These individuals presented with shorter duration of AUD, more advanced liver fibrosis on FibroScan, higher MELD scores and more frequent hepatology admissions following psychiatric hospitalization. A prior history of bariatric surgery was independently associated with presumed compensated advanced chronic liver disease. Notably, one fifth of bariatric patients self-reported excessive alcohol use even before their procedure. These findings emphasize the need for close collaboration between psychiatry and hepatology in the follow-up of bariatric patients.

ADIPOSE TISSUE INSULIN RESISTANCE IS A MARKER AND A MAJOR DRIVER OF SEVERE MASH. N. Beyene (1), J. Haas (2), S. Sabatini (3), W. Kwanten (4), A. Driessen (5), E. Dirinck (6), B. Staels (2), C. De Block (6), S. Francque (7), A. Gastaldelli (3), L. Vonghia (7) / [1] Laboratory of Experimental Medicine and Paediatrics, University of Antwerp, Antwerp, Belgium, Laboratory of Experimental Medicine and Paediatrics, University of Antwerp, Antwerp, Belgium, [2] Université de Lille, Lille, France, Université de Lille, Inserm, CHU Lille, Institut Pasteur de Lille, U1011 - EGID, Lille, France, [3] Institute of Clinical Physiology, Pisa, Italy, Metabolic Diseases Research Group and Multi-Omics Mass Spectrometry Lab, Institute of Clinical Physiology, CNR, Pisa, Italy, [4] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Department of Gastroenterology and Hepatology, Antwerp University Hospital, Antwerp, Belgium, [5] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Department of Pathology, Antwerp University Hospital, Antwerp, Belgium, [6] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Department of Endocrinology, Diabetology and Metabolic Diseases, Antwerp University Hospital, Antwerp, Belgium, [7] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Department of Gastroenterology and Hepatology, Antwerp University Hospital, Antwerp, Belgium.

Introduction: Adipose tissue insulin resistance (ADIPO-IR index) with excess free fatty acids (FFA, due to impaired suppression of lipolysis) is linked to the severity of fibrosis in metabolic dysfunction-associated steatotic liver disease (MASLD). However, whether and how ADIPO-IR marks the severity of metabolic dysfunction-associated steatohepatitis (MASH) and of hepatic inflammation is still unknown.

Aim: We aimed to determine whether ADIPO-IR is an independent predictor of MASH and fibrosis and to explore its links with hepatic inflammation and response to intervention.

Methods: The cohort included 375 individuals without a diagnosis of diabetes at enrollment with liver biopsies categorized as MASH n=219, No-MASH n=104 (including MASL n=64) and CT n=52 (healthy liver) and liver transcriptomics in a subgroup. Participants were also characterized for ADIPO-IR (FFAxInsulin), waist-to-height ratios (Waist/height), visceral (VAT) and subcutaneous adipose tissue (SAT) by computed tomography, glucose tolerance by OGTT and PNPLA3 variants. A subgroup underwent liver transcriptomic analysis. An intervention subgroup with severe obesity was followed for 12 months after receiving either bariatric surgery (BS, n=34) or lifestyle intervention (LS, n=37), with post-intervention histology to identify MASLD responders and non-responders. Logistic regression was conducted to assess ADIPO-IR as a predictor of MASH and fibrosis at baseline, adjusted for age, gender, and BMI. Multivariate linear regression was used to evaluate predictors of change in ADIPO-IR, adjusted for interventions.

Results: Subjects with MASH, no-MASH, or CT had comparable BMI (38.2-39.5 kg/m²) and SAT (p>0.05), but MASH and no-MASH had higher waist/height and VAT compared to CT (p<0.05). ADIPO-IR increased with the severity of steatosis, inflammation, and fibrosis. After adjusting for age, sex, and BMI, ADIPO-IR independently predicted the presence of MASH (OR=1.72, p=0.003) and significant fibrosis (OR=1.92, p=0.004). PNPLA3 variant carriers had similar ADIPO-IR. Liver transcriptomic analysis revealed that ADIPO-IR was positively correlated with the enrichment of gene sets related to inflammatory and immune responses, including neutrophil degranulation and interferon-gamma signalling. Post-intervention, ADIPO-IR was significantly reduced (p<0.0001), and reduction below the overall median (FU/baseline=0.4877) was more prevalent in the BS group (67.6% vs. 32.4% for LS) and in MASLD responders (60.5% vs. 32.1% for non-responders). Regardless of the intervention type, the change in waist/height was a significant predictor of the change in ADIPO-IR.

Conclusions: ADIPO-IR is an independent predictor of both MASH and significant fibrosis in MASLD. Its correlation with hepatic inflammatory gene expression, combined with its significant reduction following histologic improvement, highlights ADIPO-IR as a key marker and driver of MASH.

EPIDEMIOLOGY OF HEPATITIS DELTA VIRUS IN BELGIUM: A PROSPECTIVE CROSS-SECTIONAL COHORT STUDY. M. Coessens (1), I. Roukaerts (2), F. Lemaitre (2), J. Wawrzyniak (3), M. Steverlynck (4), M. Reda (5), M. De Vos (6), M. Reynders (7), H. Orlent (8), H. Vanpoucke (9), C. De Vloo (10), M. De Spiegeleer (11), J. Van Acker (11), T. Banica (12), E. Padalko (12), L. Lasser (13), H. Besse (14), A. Scohy (15), G. Zorzi (15), N. Yin (16), C. Moreno (17), S. Goes (18), A. Van Dalem (18), P. Beckers (19), M. Hayette (19), S. Vandamme (20), S. Van den Wijngaert (16), J. Mulkay (21), N. Van Gasse (22), P. Bruynseels (22), K. Hoet (22), B. Van Herendaal (22), W. Verlinden (23), M. Mukovnikova (24), A. Vodolazkaia (24), S. Van Gucht (2), T. Vanwolleghem (25) / [1] Laboratory of Experimental Medicine and Paediatrics, University of Antwerp, Antwerp, Belgium, Viral hepatitis research group, [2] Sciensano, Brussels, Belgium, Infectious

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Introduction: Hepatitis delta virus (HDV)-hepatitis B virus (HBV) coinfection is the most severe form of viral hepatitis, causing rapidly progressive liver disease. The 2023 EASL guidelines recommend HDV antibody (HDVAb) screening in all hepatitis B surface antigen (HBsAg) positive patients. The entry inhibitor bulevirtide has been recently approved by the European Medicines Agency and is available in several European countries. Other antiviral molecules are in advanced stages of clinical development, supporting prospective screening and linkage to care.

Aim: This multicentre, prospective, cross-sectional study aims to systematically assess HDV seroprevalence and HDV viremic rate in HBsAg-positive patients in Belgium, as well as circulating HDV genotypes. Secondary research objectives include the association between HDV seroprevalence/viremia and epidemiological, virological, and liver parameters, as well as the sensitivity of HDV antibody testing in immunocompromised patients and patients suspected of having an acute HBV-HDV coinfection.

Methods: Fifteen Belgian hospitals (high-volume centres that have diagnosed HBV-HDV coinfecting patients in the past), geographically distributed across the country, were selected to participate in this national HDV seroprevalence study. During the study period (11/25/2024 – 10/27/2025), clinical biologists at the participating hospitals sent all consecutive serum samples testing positive for HBsAg to the National Reference Centre for Viral Hepatitis (NRC, Sciensano), for double HDV reflex testing using the DiaSorin HDVAb ELISA assay (n=2000 HBsAg+ patients, balanced by hospital size). HDV PCR was performed in HDVAb+ patients with RealStar kit 1.0 (Altona Diagnostics). In addition, systematic HDV RNA screening is performed for all immunocompromised patients [e.g. patients with haematological malignancies, transplant recipients, people living with HIV (human immunodeficiency virus), and patients taking immunosuppressive medication], as well as for all patients suspected of having an acute HBV-HDV co-infection [defined as HBsAg-positive for less than six months, and one of the following: clinician-reported suspicion of acute HBV infection, positive HBcAb IgM (hepatitis B core antibody), or ALT greater than 500 U/L], irrespective of the HDV serology result. HDV genotyping was performed according to the method described by Le Gal et al (2017). Demographic, virological and liver parameters are documented.

Results: In total, 2160 HBsAg-positive patients were enrolled. HDV seroprevalence is 6.02% (n=130/2160; 5.07% - 7.13%). Out of 130 HDVAb-positive patients, 50 tested HDV RNA positive. Next to that, 75 immunocompromised patients and 18 patients suspected of having an acute HBV-HDV coinfection, were screened for HDV RNA. One coinfecting HBV-HIV+ patient tested HDV RNA positive (Ct=36.56), despite a negative HDVAb serology. HDV viraemic prevalence for the entire cohort is therefore 2.36% (n=51/2160; 1.79% - 3.12%). To date, 34 patients have been found to have genotype 1, while nine have been found to have genotype 5. HDV genotyping is still ongoing for eight patients. Compared to HDVAb-negative patients, HDVAb-positive patients were more often female (40.6% vs 56.8%, p=0.007, n=1022), were more likely to be HCV coinfecting (1.6% vs 8.5%, p=0.001, n=687), had higher median AST (27.0 vs 30.0 U/L, p=0.014, n=696), ALT (27.0 vs 33.5 U/L, p=0.008, n=979) and INR (1.00 vs 1.04, p=0.030, n=708) values, and had lower median serum creatinin values (0.87 vs 0.77 mg/dL, p=0.002, n=924).

Conclusions: This national hospital-based HDV seroprevalence study shows a significant burden of HDV infection in HBsAg+ Belgian patients. More research is needed on HDV screening recommendations in HBV-HIV coinfecting patients.

-A07-

DIAGNOSTIC ACCURACY OF NON-INVASIVE DETECTION OF CLINICALLY SIGNIFICANT PORTAL HYPERTENSION. Z. Gadi (1), R. Hajj (2), E. Ehomah (3), L. Flores Ribeiro (4), L. Schoenmakers (1), L. Vonghia (1), W. Kwanten (1), T. Vanwolleghem (1), S. Francque (1) / [1] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology & Hepatology, [2] American University of Beirut (AUB) Faculty of Medicine, Beirut, Lebanon, Beirut, Lebanon, Faculty of Medicine, [3] University of Ghana Medical school, Accra, Ghana, Ghana, Andorra, Medical school, [4] Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, Lisbon, Portugal, Faculdade de Medicina.

Introduction: Portal hypertension is central to the progression of chronic liver disease, yet its reference standard assessment by hepatic venous pressure gradient (HVPG) remains invasive and limited to specialised centres. A wide range of non-invasive tests (NITs) including elastography-based models and serum-derived scores have been proposed to predict portal pressure and identify clinically significant portal hypertension (CSPH). However, comparative data across a broader, real-world population that includes all major liver disease aetiologies are limited.

Aim: To compare the diagnostic accuracy of established portal hypertension-specific or fibrosis-related NITs against HVPG for detecting portal hypertension (PH) and CSPH in a large single-centre cohort.

Methods: Four hundred and forty-six patients were retrospectively included in whom HVPG measurement using the balloon occlusion technique and transjugular liver biopsies were performed between January 2018 and December 2024. The cohort included diverse aetiologies: MASLD (123; 27.6%), alcohol-related liver disease (129; 28.9%), metALD (28; 6.3%), viral hepatitis (20; 4.5%), and other causes (32.7%). PH and CSPH were defined as HVPG ≥ 5 mmHg and ≥ 10 mmHg respectively. The evaluated models included NICER, MODEL-3P, MODEL-5P, ANTICIPATE and ANTICIPATE-NASH, LSPS, Lok, FIB-4+, FIB-4, MAF-5, APRI, Forns Index, AGILE3+ and AGILE4. Area under the receiver operating characteristic curve (AUC), sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated.

Results: Across all aetiologies, PH was present in 345 patients (77%) and CSPH in 230 (52%). For PH detection, models with inadequate sample size because of missing values (MAF-5 and MODEL-5P) were excluded from further analysis. The remaining NITs showed good-to-excellent discrimination (AUC > 0.80) for the diagnosis of PH. NICER achieved strong balanced accuracy (AUC 0.903; sensitivity 0.80; specificity 0.84; PPV 0.95). FIB-4+ offered the highest sensitivity (0.97) and high NPV (0.75), while Lok provided the best NPV among highly sensitive models (0.64). ANTICIPATE-NASH, AGILE4, LSPS and FIB-4 (AUC range 0.860–0.887) also performed well, with specificities up to 0.90 and PPVs above 0.90. For CSPH, several models exceeded AUC 0.90. NICER remained robust (AUC 0.909; sensitivity 0.89; specificity 0.77; NPV 0.87). ANTICIPATE-NASH provided near-perfect sensitivity and NPV (0.99 each), while elastography-integrated tools such as AGILE4 (AUC 0.920) and AGILE3+ (AUC 0.911) demonstrated excellent rule-out capability (NPVs > 0.95). Classical fibrosis scores (FIB-4, APRI, Forns) showed considerably lower accuracy (AUC 0.721–0.781) with reduced specificity.

Conclusions: Across diverse liver disease aetiologies, NITs specifically developed for portal hypertension or incorporating elastography outperformed traditional fibrosis-oriented scores for detecting PH and CSPH. Models such as NICER, AGILE4 and ANTICIPATE-based tools demonstrated high diagnostic accuracy, reinforcing their suitability as non-aetiology specific practical alternatives to invasive HVPG in routine stratification and research settings.

-A08-

METABOLIC AND BARIATRIC SURGERY AND THE RISK OF ALCOHOL USE DISORDER: A SYSTEMATIC REVIEW AND META-ANALYSIS. A. Verhelst (1), J. Huau (1), Y. Van Nieuwenhove (2), L. Onghena (3), L. Devisscher (4), S. Raevens (5), X. Verhelst (5), H. Van Vlierberghe (5), A. Geerts (5), S. Lefere (5) / [1] Ghent University Hospital, Ghent, Belgium, Gastroenterology and Hepatology, [2] Ghent University, Ghent, Belgium, Human Structure and Repair, [3] AZ Sint-Lucas, Ghent, Belgium, Surgery, [4] Ghent University, Ghent, Belgium, Gut-Liver ImmunoPharmacology Unit, dpt. of Basic and Applied Medical Sciences, [5] Ghent University, Ghent, Belgium, Hepatology Research Unit, dpt. of Internal Medicine and Paediatrics.

Introduction: Metabolic and bariatric surgery (MBS) is the most effective treatment for obesity, leading to sustained weight loss and improvements in metabolic comorbidities. However, growing evidence suggests that MBS may increase the risk of alcohol use disorder (AUD). AUD is associated with rapid progression to advanced liver disease, including alcohol-related hepatitis and cirrhosis. Understanding the magnitude of this risk and identifying high-risk subgroups is crucial to optimise patient selection, preoperative counselling, and postoperative follow-up. This review focuses on Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG), the most commonly performed MBS procedures. **Aim:** The aim of this systematic review was to determine whether RYGB and SG increase the risk of AUD among adult MBS patients and to identify high-risk subgroups.

Methods: A systematic search was conducted in MEDLINE, Embase, Web of Science, and the Cochrane Library using combinations of terms related to MBS and alcohol use. Observational studies reporting on RYGB or SG were included. Two reviewers independently screened articles using Rayyan and extracted data on AUD prevalence, cumulative incidence, and risk factors. Pooled prevalence and cumulative incidence estimates were calculated using random-effects meta-analyses. Meta-regression was performed to assess the influence of time since surgery and procedure type, with preoperative values as baseline. Narrative synthesis was performed when meta-analysis was not feasible due to heterogeneity in outcome measures (e.g. ORs and HRs) or a limited number of studies. This review was conducted in accordance with the PRISMA 2020 guidelines.

Results: Thirty-three studies were included. The pooled prevalence of AUD was 7% (95% CI 0.05–0.11) for follow-up <2 years and 16% (95% CI 0.12–0.22) for ≥ 2 years. A subgroup analysis limited to RYGB patients showed a similar pattern, with the pooled prevalence increasing from 7% (95% CI 0.06–0.08) to 19% (95% CI 0.14–0.25), indicating that the overall rise was primarily driven by RYGB. The cumulative incidence of new-onset AUD was 9% (95% CI 0.05–0.16). Meta-regression demonstrated a significant time-dependent increase in postoperative AUD risk. For RYGB, the risk difference increased by approximately 0.9 percentage points per year ($\beta = 0.0094$, 95% CI 0.0062–0.0127, $p < 0.0001$). For SG, a smaller yet significant annual increase was observed ($\beta = 0.0054$, 95% CI 0.0023–0.0085, $p = 0.0006$). The difference between slopes did not reach statistical significance ($p = 0.076$). Analyses stratified by type of surgery confirmed that RYGB was consistently associated with a higher risk of AUD compared with various control groups (pooled adjusted HR 2.69, 95% CI 2.15–3.37, $p < 0.00001$), whereas SG showed no statistically significant increase (HR 0.99, 95% CI 0.67–1.45, $p = 0.94$), with some studies suggesting a reduced risk. Key risk factors identified across studies included preoperative AUD, binge-eating disorder, and smoking (particularly after RYGB). Poorer mental health and lower cognitive restraint were also associated with increased risk, whereas higher educational attainment appeared protective. Evidence for sex- and age-related susceptibility was inconsistent. Considerable heterogeneity was present, reflecting variations in study design, diagnostic tools, follow-up duration, and surgical procedures.

Conclusions: MBS, particularly RYGB, is associated with a time-dependent increase in AUD risk relative to baseline, whereas evidence for SG remains limited and less consistent. Standardised diagnostic tools and long-term follow-up are essential to better characterise high-risk populations and mitigate the risk of postoperative AUD.

-A09-

SERUM GLYCOMICS INCREASE THE PROGNOSTIC VALUE OF THE GLOBAL PBC SCORE IN PATIENTS WITH PBC: AN INTERNATIONAL MULTICENTRIC STUDY. X. Verhelst (1), N. Somers (2), E. Butaye (2), L. Grossar (2), D. Nicolas (2), A. Geerts (2), S. Raevens (2), H. Van Vlierberghe (2), V. Lygoura (3), A. Van der Meer (4), M. Van Hooff (4), G. Dalekos (3), N. Gatselis (3), B. Hansen (4) / [1] Ghent University Hospital, Ghent, Belgium, Gent, Belgium, Department of Gastroenterology and Hepatology, [2] Ghent University Hospital, Ghent, Belgium, Gent, Belgium, Gastroenterology and Hepatology, [3] General University Hospital of Larissa, Greece, Larissa, Greece, Department of Medicine and Research Laboratory of Internal Medicine, [4] Erasmus MC, University Medical Centre Rotterdam, The Netherlands, Gastroenterology and Hepatology.

Introduction: Primary Biliary Cholangitis (PBC) is a rare chronic autoimmune disease that gradually destroys the bile ducts in the liver. Prognostic scores are useful to guide treatment in patients with PBC. However, the role of biomarkers is unclear.

Aim: We studied the applicability of serum glycomic profiling in association with disease progression and liver transplant-free survival (TFS) in combination with the currently used PBC Globe Score.

The aim was to assess the prognostic power of serum glycomics in association with TFS and compare its performance to the currently used biochemical response scores like the PBC Globe score.

Methods: In this large multicentric international study, we used stored serum samples of 858 PBC patients, collected prospectively by three expert centres of the GLOBAL PBC Study Group. Whole serum N-glycomic analysis was performed using DNA sequencer assisted-Fluorophore Assisted Carbohydrate Electrophoresis (DSA-FACE). Uni- and multivariate Cox regression analyses were conducted to develop the prognostic GlycoPBCScore, with associated Kaplan Meier survival analysis. The GLOBE score and UK-PBC risk score for prediction of TFS were calculated. Cross-validation was performed.

Results: Patients had a mean follow-up of 6.43 years since sample collection, with an overall 5- and 10-year TFS of 91.6% and 83.1%, respectively. Cox regression analysis revealed increased fucosylated glycans (NA2FB, NA3Fbc, NA4Fb) and decreased bi-, and tri-antennary glycans (NA2F, NA3) in patients with poor TFS, from which the GlycoPBCScore was derived with an area under the curve (AUC) of 0.82 (95% CI [0.78-0.86], $p < 0.001$) and a hazard ratio (HR) of 3.36 (95% CI [2.82-4.01], $p < 0.001$). Patients with a score above the cut-off value of -1.9 showed an increased risk of poor 5- and 10-year TFS, compared with patients with low values ($p < 0.001$). Furthermore, patients in the 'high risk' group developed more liver cirrhosis (15.5% vs 6.3%, $p < 0.001$), hepatic decompensation (41.4% vs 15.9%, $p < 0.001$), hepatocellular carcinoma (3.2% vs 0.6%, $p = 0.003$) and had a higher mortality rate (37.4% vs 6.6%, $p < 0.001$), when compared to the 'low risk' group. In addition, the precision for TFS estimation of both the GLOBE and UK-PBC risk scores at time of sample collection showed an AUC of 0.75 (95% CI [0.71-0.80], $p < 0.001$). Other risk factors for poor TFS were high total bilirubin and alkaline phosphatase levels, together with low albumin and platelet count - which are signs of severe liver disease. When the GlycoPBCScore was adjusted for these covariates in a multivariable Cox proportional hazards model, the association with poor TFS was confirmed (HR 2.05, 95% CI [1.66-2.53], $p < 0.001$). Moreover, combining this new glycomics based biomarker with the currently used Globe Score increased the prognostic value, leading to a more accurate classification of patients in need of liver transplantation and patients with an uneventful disease course. In particular, a high negative predictive value of 97.3% was observed using the combination of Globe score and GlycoPBCscore.

Conclusions: The GlycoPBCScore is a prognostic biomarker for liver transplant-free survival in patients with PBC, that provides additional prognostic power if combined with the currently used PBC Globe Score. Patients with an uneventful disease course can accurately be identified and reassured. High risk patients could be proposed a more rapid escalation to second line treatment and more personalised medical follow up.

-A10-

EUROTRANSPLANT EXPERIENCE WITH MELD STANDARD EXCEPTIONS FOR HEPATOPULMONARY SYNDROME AND PORTOPULMONARY HYPERTENSION. M. Verstraeten (1), A. Jens (2), G. Berlakovich (3), M. Sternack (4), F. Braun (5), C. Den Hoed (6), B. Trotošek (7), D. Mikulic (8), T. Benkoe (9), A. Geerts (10), X. Verhelst (10), H. Van Vlierberghe (10), S. Raevens (10) / [1] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology and Hepatology, [2] Eurotransplant International Foundation, Leiden, The Netherlands, Eurotransplant, [3] Medical University of Vienna, Vienna, Austria, Division of Transplantation, [4] University Medical Centre Hamburg-Eppendorf, Hamburg, Germany, Department of Internal Medicine, [5] University Hospital Schleswig-Holstein, Campus Kiel, Germany, Sektion für Klinische Transplantationsmedizin, [6] Erasmus MC, University Medical Centre Rotterdam, The Netherlands, Department of Gastroenterology and Hepatology, [7] University Medical Centre Ljubljana, Ljubljana, Slovenia, Department of Abdominal Surgery, [8] University Hospital Merkur, Zagreb, Croatia, Centre for Solid Organ Transplantation, [9] Semmelweis University, Budapest, Hungary, Department of Surgery, Transplantation and Gastroenterology, [10] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Hepatopulmonary syndrome (HPS) and portopulmonary hypertension (PoPH) are severe pulmonary vascular complications of end-stage liver disease (ESLD) and portal hypertension. Some patients are eligible for Model for End-Stage Liver Disease (MELD) standard exception (SE) liver transplantation (LT) prioritization in Eurotransplant. Although the SE policy aims to ensure equitable access to transplantation, contemporary data on its impact on waitlist and post-transplant outcomes across the Eurotransplant region are scarce.

Aim: This study provides an updated evaluation of outcomes in LT candidates with SE for HPS or PoPH within Eurotransplant.

Methods: We analysed Eurotransplant registry data (2006-2022) for adult LT candidates with approved SE for HPS (n=117) or PoPH (n=25), compared with 710 matched controls (matching based on age, sex, MELD score, and liver disease etiology) without SE. Outcomes included overall survival, waitlist outcomes, and post-LT survival. Survival analyses were performed using Kaplan-Meier, Cox proportional hazards, and Fine and Gray competing risks models.

Results: Overall mortality was similar between HPS and controls (HR 1.23, 95% CI 0.93 - 1.63, $p = 0.16$), but higher in PoPH (HR 1.79, 95% CI 1.06 - 3.00, $p = 0.028$). Pre-transplant mortality was comparable across groups (for HPS: HR 1.02, 95% CI 0.68 - 1.53, $p = 0.92$; for PoPH: HR 1.22, 95% CI 0.55 - 2.72, $p = 0.62$). Post-LT survival was similar for HPS and controls (HR 1.11, 95% CI 0.73 - 1.67, $p = 0.63$), but significantly poorer for PoPH (HR 2.39, 95% CI 1.17 - 4.89, $p = 0.017$). At 6 months, survival rates were 88.1% (95% CI 84.7% - 91.6%) for control patients, 92.3% (95% CI 86.6% - 98.4%) for HPS and 57.1% (95% CI 36.3% - 89.9%) for PoPH; and at 1 year 84.7% (95% CI 81% - 88.7%), 87% (95% CI 79.7% - 94.8%), and 57.1% (95% CI 36.3% - 89.9%) respectively. Infection was the leading cause of post-LT mortality; cardiovascular events were more frequent in PoPH recipients.

Conclusions: LT candidates with SE for severe HPS achieve comparable overall and post-LT survival to non-SE recipients, supporting the appropriateness of current SE policy. Conversely, PoPH patients demonstrate markedly poorer post-LT outcomes, highlighting the need for careful candidate selection, optimized pre-transplant management, and perioperative strategies to improve survival.

-A11-

FROM OUTSIDE TO INSIDE: HOW CHANGES IN ECM COMPOSITION INFLUENCE CHOLANGIOCYTES' BEHAVIOUR. R. Claus (1), I. Leclercq (1), R. Manco (1) / [1] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, GAEN.

Introduction: During the development of chronic liver disease, native hepatocytes enter replicative senescence, and cholangiocytes begin to proliferate as Ductular Reaction (DR) cells, which can eventually differentiate into hepatocytes. Increasing evidence suggests that the extracellular matrix (ECM), especially Laminin, plays a pivotal role in guiding DR cell fate. However, the mechanism by which ECM proteins such as Laminin influence cholangiocytes behaviour and identity remain to be elucidated. A known process by which mechanical cues from the microenvironment are transmitted to the nucleus, altering gene expression is called Nuclear Mechanotransduction.

Aim: Thus, in this study, we explored how ECM composition regulates cholangiocyte's identity through this process to better understand the gatekeeping of Laminin on cholangiocytes phenotype.

Methods: To be able to study the influence of ECM on cholangiocyte's identity, we used normal mouse cholangiocytes (NMC) cultures in a Double-spheroid model. This model allows us to control the ECM composition, and, in this case, we compared cell behaviour in Laminin-rich versus Collagen I-rich matrices. ECM influences on cholangiocytes behaviour were analysed through transcriptomic analysis, immunofluorescence, RT-qPCR techniques, imaging, flow cytometry and functional analysis.

Results: Imaging and transcriptomics analysis confirmed that our double-spheroid model is robust and that Laminin is the gatekeeper of cholangiocyte's phenotype. Indeed, NMC embedded in Laminin formed branches-like structure and maintained the biliary phenotype, while those embedded in Collagen I, display dispersed, unstructured spreading behaviour and stress-responsive features. Moreover, transcriptomics analysis showed ECM-specific signatures: Laminin enriched bile secretion pathways, while Collagen I triggered stress and inflammatory responses. ECM composition also affected nuclear morphology and organization. Laminin promoted smaller, rounder, stiffer nuclei and increased Laminin-associated domains (LADs), consistent with transcriptional stability. However, when cultured in Collagen I, cells had an irregular nuclear shapes and fewer LADs-indicating higher transcriptional plasticity. Noticeably, when disrupting the Nuclear Mechanotransduction signal using Y-27632, a Rho-associated coiled-coil containing protein kinase (ROCK) inhibitor, the difference observed before are lost, showing that ECM influences cell's behaviour and identity.

Conclusions: Nuclear Mechanotransduction is the central mechanism by which ECM composition influence cell fate, and in this case cholangiocyte's identity. This study offers key insights into liver regeneration and therapeutic strategies targeting DR cells by linking the microenvironment to nuclear structure and gene expression.

PREVALENCE AND RISK FACTORS OF SARCOPENIA THROUGHOUT THE DISEASE SPECTRUM OF SYMPTOMATIC POLYCYSTIC LIVER DISEASE: A RETROSPECTIVE MULTICENTRE COHORT STUDY. N. Van Horebeek (1), O. Koc (2), W. Coudyzer (3), A. Billiet (4), I. Colle (5), F. Janssens (6), S. Demaeght (7), H. Orlent (8), J. Delwaide (9), S. Decock (10), C. Devloo (11), S. Francque (12), C. Moreno (13), D. Sprengers (14), D. Monbaliu (15), J. Pirenne (15), F. Nevens (2), J. Verbeek (2) / [1] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Gastroenterology and Hepatology, [2] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Gastroenterology and Hepatology, [3] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Radiology, [4] AZ Oostende, Oostende, Belgium, Gastroenterology and Hepatology, [5] AZORG AALST, Aalst, Belgium, Gastroenterology and Hepatology, [6] Jessa Hospital, Hasselt, Belgium, Gastroenterology and Hepatology, [7] Grand Hopital de Charleroi, Charleroi, Belgium, Gastroenterology and Hepatology, [8] AZ Sint-Jan Brugge, Brugge, Belgium, Gastroenterology and Hepatology, [9] CHU Liege, Liège, Belgium, Gastroenterology and Hepatology, [10] AZ Sint-Lucas Brugge, Assebroek, Brugge, Belgium, Gastroenterology and Hepatology, [11] AZ Delta, Belgium, Gastroenterology and Hepatology, [12] Antwerp University Hospital, Edegem, Belgium, Gastroenterology and Hepatology, [13] Hôpital Erasme, ULB, Belgium, Gastroenterology and Hepatology, [14] ZAS, Antwerp, Belgium, Gastroenterology and Hepatology, [15] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Abdominal Transplant Surgery and Coordination.

Introduction: The severity of symptoms and the presence of complications such as malnutrition are key indications for volume-reducing treatment (including liver transplantation (LTx)) in patients with polycystic liver disease (PLD). Malnutrition in this population is traditionally assessed using the mid-upper arm circumference (MUAC), although the skeletal muscle index at the third lumbar vertebra (SMI-L3) on computed tomography is increasingly recognized as a more accurate marker. Recently, the United Network for Organ Sharing in the United States accepted sarcopenia as a standard exception criterion for liver transplantation. However, the prevalence and risk factors of sarcopenia in symptomatic PLD remain unclear.

Aim: This study aimed to (1) determine the prevalence of sarcopenia in patients with PLD, (2) identify clinical predictors of sarcopenia, and (3) assess whether sarcopenia independently predicts the need for volume-reducing therapy.

Methods: This multicentre retrospective cohort study included 296 adult patients with symptomatic PLD, either isolated or associated with autosomal dominant polycystic kidney disease (ADPKD). Sarcopenia was defined using SMI-L3 on CT: $<39 \text{ cm}^2/\text{m}^2$ for females and $<50 \text{ cm}^2/\text{m}^2$ for males. Reference values for MUAC were $<23.1 \text{ cm}$ for females and $<23.8 \text{ cm}$ for males. Additional variables included demographics, presence of ADPKD, BMI, height-adjusted total liver volume (htLV), symptom severity (POLCA score), creatinine levels and Charlson Comorbidity Index. Associations between sarcopenia and therapeutic needs (somatostatin analogue, surgical intervention, or LTx) were assessed using univariate tests and multivariable logistic regression adjusting for confounders (age, sex, BMI, ADPKD, malnutrition, POLCA score, htLV, creatinine levels and Charlson Comorbidity Index).

Results: Patients were mostly female (82.4%) with a median age of 54 years. The majority of PLD patients (216/296; 73.0%) had ADPKD. SMI-L3 data were available for 137/296 (46.3%) patients of whom 80 (58.3%) had sarcopenia. Patients with and without sarcopenia showed no significant differences in median age (50 ± 16 vs 51 ± 17 years, $p = 0.937$), prevalence of ADPKD (83.8% vs 84.2%, $p = 0.942$), malnutrition assessed by MUAC value (39.4% vs 32.6%, $p = 0.463$), total POLCA score (22 ± 18 vs 20 ± 17), htLV ($2667 \pm 1675 \text{ mL}$ vs $2539 \pm 2048 \text{ mL}$), or Charlson Comorbidity Index ($2 + 3$ vs $3 + 4$, $p\text{-value} = 0.237$). There was a significant difference in BMI ($22 + 4$ vs $24 + 5 \text{ kg/m}^2$, $p\text{-value} = 0.009$) and creatinine levels ($1.01 + 0.63$ vs $1.14 + 3.05 \text{ mg/dL}$, $p\text{-value} = 0.040$) among patients with and without sarcopenia. In multivariable analysis, only BMI (OR: 0.812, CI 0.695 – 0.948, $p\text{-value} = 0.008$) was an independent predictor for the presence sarcopenia. The overall need for volume-reducing therapy was high (86.8%): somatostatin analogue (46.7%), resection/sclerotherapy (11.0%), and LTx (126/269, 46.8%) (multiple treatments were possible). After multivariable adjustment, sarcopenia independently predicted the need for volume-reducing therapy (OR 8.49, 95% CI 1.53–53.39, $p\text{-value} = 0.018$), alongside htLV (OR 1.001, $p\text{-value} = 0.038$) and Charlson Comorbidity Index (OR 2.56, $p\text{-value} = 0.033$).

Conclusions: Sarcopenia is highly prevalent in patients with symptomatic PLD. Together with htLV sarcopenia predicts the need for volume-reducing therapy, whereas MUAC does not. Therefore, we recommend prioritizing sarcopenia measured by CT based L3-SMI over MUAC in the follow up and management of PLD patients, especially in determining transplant eligibility.

ULTRASTRUCTURAL ASSESSMENT OF LIVER SINUSOIDAL ENDOTHELIAL CELL (LSEC) CAPILLARISATION IN METABOLIC-DYSFUNCTION ASSOCIATED STEATOTIC LIVER DISEASE (MASLD) AND ITS MODULATION BY LANIFIBRANOR. S. Chotkoe (1), G. Wettstein (2), J. De Man (3), S. Thys (4), I. Pintelon (5), Y. Lu (3), N. Beyene (6), J. Junien (2), D. Van der Graaff (7), B. De Winter (6), W. De Vos (5), L. Vonghia (8), W. Kwanten (9), S. Francque (8) / [1] Universiteit Antwerpen / Antwerp University Hospital, WILRIJK (Antwerpen), Belgium, Translational Research in Immunology and Inflammation (TWI²N), [2] Inventiva Pharma, Daix, France, Biology and Pharmacology, [3] University of Antwerp, Antwerp, Belgium, Translational Research in Immunology and Inflammation (TWI²N), [4] University of Antwerp, Antwerp, Belgium, Department of Veterinary Sciences, [5] University of Antwerp, Antwerp, Belgium, Department of Veterinary Sciences, [6] University of Antwerp/Antwerp University Hospital, Edegem, Belgium, Translational Research in Immunology and Inflammation (TWI²N), [7] Antwerp University Hospital, Edegem, Belgium, Gastroenterology and Hepatology, [8] University of Antwerp/Antwerp University Hospital, Edegem, Belgium, Gastroenterology and Hepatology, [9] Universiteit Antwerpen / Antwerp University Hospital, WILRIJK (Antwerpen), Belgium, Gastroenterology and Hepatology

Introduction: In metabolic dysfunction-associated steatotic liver disease (MASLD), intrahepatic vascular resistance (IHVR) increases in early stages, driven by liver sinusoidal endothelial cell (LSEC) dysfunction and their loss of fenestrae (capillarisation). This phenomenon contributes to disease progression. The pan-peroxisome proliferator-activated receptor (pan-PPAR) agonist lanifibranor has demonstrated beneficial effects on liver histology in patients with MASLD and was also shown to have favourable effects in preclinical models of cirrhosis and portal hypertension. We previously demonstrated that lanifibranor normalised increased IHVR in a rat model of isolated steatosis by improving liver histology and primarily restoring both the structural and functional intrahepatic vascular alterations. **Aim:** This study aimed to 1) explore ultrastructural sinusoidal remodelling across the human MASLD spectrum, 2) assess the effects of lanifibranor on LSEC fenestrae at histological and ultrastructural levels in a rat model of early MASLD, 3) and histologically evaluate the progression of LSEC capillarisation over time in a mouse model of MASLD.

Methods: Human liver biopsy samples (n = 13) across the full MASLD spectrum were evaluated by transmission electron microscopy (TEM). Male Wistar rats (n = 8/group) were fed a methionine-choline-deficient diet (MCDD) or control diet (CD) for 4 weeks and received simultaneously placebo or lanifibranor (100 mg/kg/day) via oral gavage QD. Rat livers were evaluated by CD34 immunostaining, TEM, and scanning electron microscopy (SEM) with quantitative analysis of fenestrae. Evolution of capillarisation over time was also explored by CD34 immunostaining in a second model using C57BL/6 mice (n = 6/group) fed either CD or a high-fat high-fructose diet (HFHFD) at 24, 36 and 44 weeks.

Results: On biopsies, non-MASLD liver displayed normal fenestrated sinusoids. Early MASL (F1-2) retained fenestrae but developed basement membrane fragments and perisinusoidal fibrosis. In steatohepatitis (F2-F3) LSEC thickening and loss of fenestrae occurred. Cirrhosis exhibited complete capillarisation. Placebo-treated MCDD-fed rats compared to CD-fed rats showed increased CD34 staining (38.8 ± 2.5 vs. 20.9 ± 2.8 , $p < 0.001$), and ultrastructurally, increased fenestrae diameters, reduced fenestrae frequency (7.2 ± 0.4 vs. 10.8 ± 0.3 , $p < 0.0001$) and LSEC porosity (5.7 ± 0.4 vs. 7.5 ± 0.2 , $p < 0.01$). In MCDD-steatosis, lanifibranor decreased CD34 staining (21.4 ± 5.7 vs. 38.8 ± 2.5 , $p < 0.05$) and restored fenestrae frequency (9.3 ± 0.3 vs. 7.2 ± 0.4 , $p < 0.01$) and LSEC porosity (7.2 ± 0.3 vs. 5.7 ± 0.4 , $p < 0.01$) to levels comparable with controls. In HFHFD-fed mice, CD34 staining increased with diet duration, reaching significant elevations at 36 and 44 weeks.

Conclusions: Across species, LSEC capillarisation develops early in MASLD, albeit heterogeneously, and progresses with disease severity. Lanifibranor restores LSEC (ultra)structure in early MASLD, highlighting its therapeutic potential to restore vascular alterations and beneficially influence disease progression.

IMMUNOTHERAPY AS A BRIDGE TO LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA, A MULTICENTRIC EXPERIENCE. M. Messaoudi (1), O. Detry (2), L. Vonghia (3), H. Van Vlierberghe (4), T. Chapelle (5), E. Bonaccorsi-Riani (6), C. Amicone (7), H. Eker (8), C. Francoz (9), I. Borbath (1), G. Dahlqvist (10) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'hépatogastroentérologie, [2] CHU Liege, Liège, Belgium, Service de chirurgie et transplantation, [3] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Hepatogastroenterology department, [4] University

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Introduction: Immune-checkpoint inhibitors (ICIs) increasingly downstage hepatocellular carcinoma (HCC) to liver transplantation (LT), but their sustained immune activation may heighten the risk of graft rejection when given before or after transplant. Evidence remains limited to small and heterogeneous studies, suggesting higher rejection rates with short wash-out intervals. More data are needed to define safe timing and immunosuppression strategies around transplantation in ICI-exposed patients. Therefore, real-world multicentre data are needed.

Aim: We aim to evaluate the impact of immunotherapy on graft outcomes, the risk for rejection and post-transplant HCC recurrence.

Methods: We retrospectively collected data from patients treated with ICIs between January 2020 and October 2025 who underwent liver transplantation in all transplant centres in Belgium and in Beaujon Hospital, Paris. We collected demographic data, pre-transplant HCC characteristics (number and size of nodules, alpha-fetoprotein levels), and post-transplant outcomes.

Results: We collected data from 15 patients. The cohort consisted predominantly of men (80%), with a mean age at LT of 55.6 ± 12.3 years. Cirrhosis was mainly of viral origin (40%), and alcohol-related liver disease accounted for 20%. The mean MELD score was 12.1 ± 4.3 , and most patients were classified as Child–Pugh A. The mean ALBI score was -2.2 ± 0.8 . At HCC diagnosis, patients had on average 2.1 nodules, and the median size of the largest lesion was 55 mm (range 24–119). BCLC stage was B in most patients (80%), while two were classified as BCLC C and one as BCLC D. Mean alpha-fetoprotein at LT was 29.9 ng/mL. All but one patient received Atezolizumab plus Bevacizumab before LT. One patient received Durvalumab for a mixed HCC–iCCA lesion with predominant intrahepatic cholangiocarcinoma features. The median washout period between immunotherapy and LT was 5 months (range 1–23). The mean interval between HCC diagnosis and LT was 27.4 ± 19.6 months. Six patients (40%) underwent additional bridging therapies (radio- or chemoembolization, external radiotherapy, microwave ablation, etc.). On the liver explants (N = 12), 30% were classified as disease-free (pT0N0) and 30% as pT1 (a or b) N0. Two patients were pT2N0 and two were pT3N0. After a median follow-up of 10 months (range 1–32), two patients developed recurrence at 5.5- and 13-months post-LT, respectively. One patient had been classified as pT3N0 and the other as pT1bN0 with poorly differentiated HCC. The latter patient died from oncological progression despite salvage chemo and immunotherapy. Early allograft rejection within the first postoperative month occurred in two patients, both successfully treated with steroids. Among the 11 patients with available data on induction therapy, 8 received Basiliximab. Six patients are currently maintained on tacrolimus monotherapy without additional immunosuppressive agents.

Conclusions: Immunotherapy prior to liver transplantation appears feasible in carefully selected patients, with acceptable rates of rejection and early post-transplant outcomes. In our cohort, ICIs effectively contributed to tumour control and downstaging, enabling access to LT in patients with advanced HCC. However, longer follow-up and larger prospective studies are required to better assess the long-term risk of recurrence and to refine optimal timing and immunosuppression strategies in ICI-exposed candidates.

-A15-

THE NATURAL HISTORY OF PORTO-SINUSOIDAL VASCULAR DISORDER WITHOUT PORTAL HYPERTENSION: A MULTICENTRE RETROSPECTIVE VALDIG STUDY. E. Kaze (1), S. Raevens (2), G. Dahlqvist (3), M. Saracco (4), L. Moga (5), N. Pugliese (6), E. Farina (7), E. Murcia (8), L. Balcar (9), C. Boros (10), M. Lucà (11), L. Argiento (12), H. Giudicelli (13), T. Vanwolleghem (14), A. Driessen (15), S. Shalaby (16), W. Ramírez-Quesada (16), D. Tazibt (17), O. Gorla (18), L. Elkrief (19), J. Delwaide (20), A. Marot (21), Q. Schoevaerdt (21), C. Moreno (1), J. Cervoni (17), V. Hernandez-Gea (16), J. Garcia-Pagan (16), S. Francque (14), D. Thabut (13), C. Cafasso (22), M. Ziol (23), P. Nahon (10), G. Semmler (9), B. Scheiner (9), C. Bureau (8), M. Vigano (7), A. Loglio (7), A. Aghemo (6), A. Plessier (24), P. Rautou (24), P. Baldin (25), L. Verset (26), A. Hoorens (27), P. Deltenre (28) / [1] CUB Hôpital Erasme, Belgium, Department of Gastroenterology, Hepatology and Digestive Oncology, [2] University Hospital Ghent (UZ Gent), Gent, Belgium, Liver Research Centre Ghent, [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Brussels,

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Introduction: Data on the natural history of patients with histological lesions of a porto-sinusoidal vascular disorder (PSVD) who do not show signs of portal hypertension (PH) are scarce.

Aim: Describe the natural history of these patients and identify risk factors for disease progression.

Methods: A retrospective study was conducted to collect health-related data on patients with a histopathological diagnosis of PSVD and no signs of PH, across 17 Vascular Liver Disease Group (VALDIG) centres. Patients with a platelets count $<150,000/\text{mm}^3$, a splenomegaly $>130\text{ mm}$, ascites, esophageal or gastric varices, or any other obvious portosystemic collateralization were excluded. The liver tissue sample should be at least 15 mm long. A central review of the liver tissue sample had not yet been performed at this stage. According to previous definitions, associated conditions were defined as the use of any medication or the presence of any immunological, haematological, congenital, or hereditary disease that could induce PSVD. Associated conditions were considered severe if they may be potentially associated with reduced life expectancy. Main endpoints were the development of PH (either ascites, obvious portosystemic collateralization, or oesophageal or gastric varices) and death.

Results: 227 patients were included (92 men [41%], median age 46 years [95% CI: 43-50]). Indication for liver tissue sampling was abnormal liver tests in 186 patients (82%). Main laboratory values at diagnosis were as follows: AST 41 U/L (95% CI: 35-43); ALT 56 U/L (95% CI: 48-64); alkaline phosphatase 113 U/L (95% CI: 102-121); GGT 132 U/L (95% CI: 115-152); bilirubin 1 mg/dL (95% CI: 1-2); albumin 42 g/L (95% CI: 41-43); INR 1 (95% CI: 1-1); platelets count $246,000/\text{mm}^3$ (95% CI: 236,000-260,000). The length of the liver tissue sample was 31 mm (95% CI: 30-34 mm). Histological findings were nodular regenerative hyperplasia, obliterative portal veinopathy, incomplete septal cirrhosis, a combination of these histological lesions, as well as sinusoidal dilatation with or without other signs indicative of PSVD, in 126 (56%), 41 (18%), 2 (1%), 14 (6%) and 44 (19%) patients, respectively. Associated conditions were observed in 100 patients (46%), of which 55 (24%) were considered as severe. During a median follow-up of 37 months (95% CI: 27-46), 3 patients developed portal vein thrombosis. One of these patients had tumoural portal vein thrombosis related to metastatic colorectal neoplasia. Three patients (1.3%) developed PH-related manifestations (ascites in 2 patients and esophageal or gastric varices in one patient). Nineteen patients (8%) died, 17 from non-hepatic causes and two from complications related to preexisting cholangiocarcinoma. No patient died from a PH-related complication. One underwent liver transplantation for colorectal carcinoma-related liver metastasis. Compared to those who did not, patients who developed PH-related manifestations were older on average (61 vs. 45 years, $p=0.11$), had higher alkaline phosphatase level (241 vs. 111 IU/L, $p=0.016$), and similar platelets count ($245,000$ vs. $305,000/\text{mm}^3$, $p=0.3$). All patients who developed PH-related manifestations had associated conditions. The cumulative incidence of PH-related manifestations at 10 years was 6% (95% CI: 2-20%); 12% (95% CI: 4-35) in patients with an associated condition versus 0% in those without ($p=0.09$). Compared to patients who did not die, those who died were older (58 vs. 45 years, $p<0.001$), had higher AST

levels (116 vs. 38 IU/L, $p<0.001$), higher ALT levels (125 vs. 54 IU/L, $p=0.004$), lower haemoglobin levels (108 vs. 137 g/dL, $p<0.001$), lower platelets count (208,000 vs. 248,000/mm³, $p=0.05$), more frequent associated conditions (15 [79%] vs. 85[41%], $p=0.003$), and more frequent severe associated conditions (14 [74%] vs. 41 [20%], $p<0.001$). Independent predictors of death were age (relative risk [RR]: 1.07, 95% CI: 1.03, 1.11, $p<0.001$) and presence of a severe associated condition (RR: 4.76, 95% CI: 1.55–14.65, $p=0.006$). The 10-year survival rate was 84% (95% CI: 77–92%); 95% (95% CI: 89-100) in patients without an associated condition, 100% in patients with a non-severe associated condition, and 58% (95% CI: 41-76) in patients with a severe associated condition ($p<0.001$).

Conclusions: Most patients with PSVD who did not present with PH will not develop it. Sixteen per cent of patients die within 10 years, mostly from non-hepatic causes, and the risk of death is independently associated with the severity of the associated condition.

-A16-

CORTICOSTEROIDS ARE INEFFECTIVE IN INDIVIDUALS WITH SEVERE ALCOHOL-ASSOCIATED HEPATITIS AND EARLY SPONTANEOUS IMPROVEMENT: A MULTICENTRE BELGIAN RANDOMIZED PLACEBO-CONTROLLED TRIAL. C. Moreno (1), P. Deltenre (2), A. Marot (3), H. Njimi (4), L. Lasser (5), D. Degré (6), A. Hittelet (7), J. Delwaide (8), A. Geerts (9), S. François (10), B. Bastens (11), T. Gustot (6), E. Trépo (6) / [1] Erasme Hospital, Brussels, Belgium, Department of Gastroenterology and Hepatopancreato, [2] Clinique Saint-Luc Bouge ; CHU UCL Namur ; CUB Hôpital Erasme, Belgium, Department of Gastroenterology and Hepatology, [3] CHU UCL Namur, Yvoir, Belgium, Department of Gastroenterology and Hepatology, [4] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Biomedical statistics, [5] CHU Brugmann, Brussels, Belgium, Department of Hepatogastroenterology, [6] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, [7] CHU Ambroise Paré MONS, Mons, Belgium, Department of Gastroenterology, [8] CHU Liege, Liège, Belgium, Department of Hepatogastroenterology, [9] Ghent University Hospital, Gent, Belgium, Belgium, Department of Hepatogastroenterology, [10] University Hospital Brussels, Vrije Universiteit Brussel, Belgium, Department of Hepatogastroenterology, [11] Clinique MontLégia- CHC Groupe Santé, Liège, Belgium, Department of Gastroenterology.

Introduction: Severe alcohol-associated hepatitis (AH) is a life-threatening disease for which corticosteroid therapy is recommended in the absence of contraindication. A significant proportion of patients with severe AH have a spontaneous serum bilirubin decrease early after admission.

Aim: Our aim was to determine whether corticosteroid therapy is more effective than placebo in individuals with severe AH and early spontaneous improvement.

Methods: In this multicentre, randomized, controlled trial conducted between February 2018 and May 2024 in 10 Belgian hospitals, patients aged 18 or older, who were heavy drinkers, with recent onset of jaundice, with a biopsy-proven severe AH (mDF³² at admission), and with a spontaneous early improvement (i.e. serum bilirubin level decrease > 10% at day 5-10 after admission) were randomized to either corticosteroids (CS) (methylprednisolone 32 mg/d) or placebo (P) for 28 days. Primary endpoint was to compare 3-month mortality rate between both groups of treatment. Secondary endpoints were to compare 1-month mortality rate and infection rate during study period between both groups.

Results: A total of 69 patients were randomized, 38 in the corticosteroid group and 31 in the placebo group. Baseline characteristics were not significantly different between the two groups (CS vs P) for age (52 ± 8 vs. 51 ± 10), male gender (76% vs. 63%), total bilirubin ($7.4[5.1-10.8]$ vs. $9.3[6.0-17.6]$ mg/dL), INR ($1.64 [1.48-1.80]$ vs $1.70 [1.48-1.98]$), mDF at admission ($44[37-57]$ vs. $45[40-58]$) and MELD score ($21[19-23]$ vs $21[19-24]$). Decrease in bilirubin level between admission and screening was not different between both groups ($31\pm 15\%$ vs $27\pm 11\%$). Lille score at day 7 of treatment was $0.18 [0.07-0.30]$ and $0.18 [0.07-0.40]$ in CS and P group, respectively ($p>0.9$). At 3 months, the probability of survival was not different between both groups ($83[72-96]$ vs $82[69-98]$ % in CS and P groups respectively, $p=0.88$). There was no difference in the probability of 1-month survival between CS and P groups ($95[88-100]$ vs $94[85-100]$ %, $p=0.85$). Probability of infection during the study period was 48 % in the CS group and 36 % in the P group ($p=0.41$). Age and Lille score were significantly associated with 3-month survival. The study was prematurely interrupted due to a low recruitment rate.

Conclusions: The present study failed to identify any benefit from corticosteroid therapy in patients with severe AH and early decrease in bilirubin level after admission. Even if the number of included patients initially planned was not reached, it is unlikely that corticosteroids provide a survival benefit when bilirubin

level spontaneously decreases by at least 10%. Waiting five days after admission before deciding to start steroids seems to be a reasonable strategy.

-A17-

SERUM GLYCOMICS AT ADMISSION PREDICT LIVER TRANSPLANT-FREE SURVIVAL IN PATIENTS WITH ACETAMINOPHEN-INDUCED ACUTE LIVER FAILURE. L. Grossar (1), N. Somers (2), E. Butaye (3), N. Debusschere (1), T. Vanwolleghem (4), G. Dahlqvist (5), J. Delwaide (6), J. Verbeek (7), L. Devisscher (1), S. Lefere (1), L. Meuris (3), N. Callewaert (3), S. Raevens (8), A. Geerts (8), H. Van Vlierberghe (8), X. Verhelst (8) / [1] Ghent University, Ghent, Belgium, Liver Research Centre Ghent, [2] Ghent University Hospital, Ghent, Belgium, Gent, Belgium, Internal Medicine and Paediatrics, [3] VIB, Gent, Belgium, Centre for Medical Biotechnology, VIB, Ghent, Belgium., [4] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology and Hepatology, [5] Cliniques universitaires Saint-Luc, Brussels, Belgium, Brussels, Belgium, Hepatogastroenterology and Liver Transplantation, [6] CHU Liege, Liège, Belgium, Gastroenterology and Hepatology, [7] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [8] Ghent University Hospital, Ghent, Belgium, Gent, Belgium, Gastroenterology and Hepatology.

Introduction: Acute liver failure (ALF) is a rare but potentially life-threatening clinical syndrome characterized by hepatocellular damage and impaired liver function, manifesting as jaundice, coagulopathy and hepatic encephalopathy in subjects with no prior pre-existing disease. In those not responding to medical therapy, emergency liver transplantation (ELT) is required to avoid fatal outcome. The decision to list a subject for ELT is based on imperfect prediction rules with strong specificity, but limited sensitivity, thereby providing good ruling-in capacity but unacceptably poor ruling-out performance. A real clinical need exists for biomarkers with strong negative predictive value and fast turnaround-time in order to facilitate decision-making and avoid unnecessary ELT and/or referral to a transplant centre.

Aim: We aimed to assess differences in the total serum N-glycome at admission in subjects with ALF due to acetaminophen (APAP) overdose according to the outcome of emergency liver transplantation. Additionally, we aimed to derive a serum glycomics biomarker able to predict need for emergency liver transplantation.

Methods: We performed a prospective, multicentre study in five liver transplant centres in Belgium, between 2014 and 2024. All participating centres were referral centres for ELT. Decision to perform ELT was based on fulfilment of the King's College Criteria, in conjunction with judgment by the multidisciplinary transplant team. In 91 patients with APAP-related ALF, serum samples were collected within 24 hours of admission for analysis of the total serum N-glycome via DNA sequencing equipment-fluorophore assisted carbohydrate electrophoresis (DSA-FACE). Relative glycan abundancies underwent central log-ratio transformation, before comparison between outcome groups, allowing robust statistical comparison for compositional data. A glycan model to predict occurrence of liver transplantation was derived using elastic net regression, which is a penalized regression model that avoids model overfitting. The optimal cut-off for classification was determined by the Youden index.

Results: Seven out of 91 (7.7%) subjects underwent ELT, with two deaths occurring after liver transplantation. Another five (5.5%) died without undergoing prior ELT, either because an organ was not timely available, or because the procedure was deemed futile. We observed a significant increase of the agalacto, core-fucosylated glycan NGA2F and of the agalacto, core-fucosylated, bisecting glycan NGA2FB (independent samples t-test, p-values 0.0356 and 0.0239, respectively). After elastic net regression, a glycan score predictive of liver transplantation was derived, mainly characterized by a relative increase in undergalactosylation and fucosylation, and by a relative decrease in branched glycans. At the optimal cut-off of 0.0815, this biomarker predicted ELT with a sensitivity of 85.7%, specificity of 73.8%, and a negative predictive value of 98.4%. The area under the receiver operating curve was 0.833 (95% confidence interval: 0.711 – 0.955).

Conclusions: In subjects with APAP-related ALF, a distinct glycomic signature can be determined on serum samples at admission, reliably ruling-out subjects not requiring ELT. Application of this serum biomarker could prevent unnecessary liver transplantation and/or referral to tertiary care, and thus avoid significant morbidity and healthcare cost utilization.

-A18-

IMMUNE CHECKPOINT INHIBITOR-INDUCED LIVER INJURY: CORRELATION BETWEEN HISTOPATHOLOGICAL PATTERNS OF LIVER DAMAGE, TREATMENT REGIMENS, AND CLINICAL OUTCOMES. N. Brouwer (1), T. Delay (1), C. Jacobs (2), X. Verhelst (3), A. Geerts (3), H. Van Vlierberghe (4), S. Raevens (4), M. Saerens (5), A. Hoorens (6) / [1] Ghent University, Ghent, Belgium, Dept. of Diagnostic

Sciences, [2] Ghent University Hospital, Gent, Belgium, Dept. of Medical Oncology, [3] Ghent University Hospital, Gent, Belgium, Dept. of Gastroenterology and Hepatology, [4] Ghent University Hospital, Ghent, Belgium, Dept. of Gastroenterology and Hepatology, [5] Ghent University Hospital, Ghent, Belgium, Dept. of Medical Oncology, [6] Ghent University Hospital, Ghent, Belgium, Pathology.

Introduction: Although immune checkpoint inhibitors (ICIs) have revolutionised cancer therapy, they are associated with immune-related adverse events (irAEs), including immune-mediated liver injury caused by ICIs (ILICI). ILICI can be severe and may necessitate treatment discontinuation. However, diagnosis remains challenging and the progression of ILICI is difficult to predict. **Aim:** The objective of this study is to identify the characteristic histopathological features of ILICI and delineate its clinical course, to support accurate diagnoses and informed therapeutic decisions. **Methods:** We conducted a retrospective cohort study of liver biopsies performed for suspected ILICI. Data were systematically extracted from pathology reports and electronic medical records. The primary outcomes were the histopathological patterns of liver injury, the response to corticosteroid therapy and the evolution of the disease.

Results: The study included 106 liver biopsies obtained for suspected ILICI. Following exclusion of 9 cases unrelated to ICI therapy and 2 cases confounded by prior immunosuppression, the diagnostic cohort consisted of 83 patients. Among these, 60 patients with complete clinical and histopathological information constituted the clinical cohort, whereas 23 referral cases lacked full follow-up. Repeat biopsies were performed in 11 patients, including 11 second and 1 third biopsy. Specific histopathological features of ILICI are lacking, consistent with the broader challenges of functional liver pathology. As a result, clinical correlation—particularly assessment of treatment response—remains indispensable for accurate diagnosis. Nevertheless, analysis of our cohort revealed that in a subset of patients, ILICI could be reliably excluded through biopsy evaluation. Approximately 10% of cases were ultimately classified as non-irAE liver injury, primarily guided by biopsy results. In the cohort of confirmed ILICI, 56.6% of patients exhibited pure hepatitis, 16.9% pure cholangiopathy, and 24.1% mixed features, correlating with biochemical profiles. The hepatitis component most often manifested as panlobular hepatitis (56.7%), occasionally accompanied by numerous microgranulomas (10.5%). Centrilobular hepatitis occurred in 25.4% of cases, steatohepatitis in 7.5%, and granulomatous hepatitis with epithelioid granulomas in 6%. An autoimmune hepatitis-like pattern with interface hepatitis was virtually absent. Severe hepatitis was documented in 9% of patients. Cholangiopathy was identified in 41.0% of cases. One patient developed hemophagocytic lymphohistiocytosis. Of the patients, half received PD-1/PD-L1 inhibitors and half received PD-1/PD-L1 plus CTLA-4 combination therapy. Notably, only about 10% of patients with a mixed histopathological pattern had received combination therapy. Hepatitis demonstrated a favourable response to immunosuppression (60.4%), whereas cholangiopathy was more refractory, with one patient progressing to secondary sclerosing cholangitis. Immunotherapy was resumed in 25% of patients, yet relapse occurred in 45.5% of these. Relapse was also documented in some patients without rechallenge. Follow-up biopsies in hepatitis cases revealed that histological improvement or progression did not reliably correlate with steroid response. In contrast, persistent or newly developed cholangiopathy features were consistently linked to steroid resistance. Notably, even when cholangiopathy resolved and steroids proved effective, all such patients experienced recurrence of ILICI.

Conclusions: Immune-related liver injury (ILICI) can manifest through a spectrum of histopathological patterns. Certain features, such as panlobular hepatitis with numerous microgranulomas and cholangiopathy, can support diagnosis. Panlobular hepatitis with numerous microgranulomas is rarely observed in other aetiologies, while cholangiopathy represents an uncommon manifestation of drug-induced liver injury (DILI) once amoxicillin-clavulanic acid is excluded. Most cases are manageable, but steroid-refractory disease requires timely escalation to second-line therapy. Vigilant monitoring is essential given the risk of relapse, even after treatment cessation. Although chronic liver injury is generally rare following ILICI, one patient developed secondary sclerosing cholangitis with advanced fibrosis. Another patient experienced HLH, an exceptionally rare yet severe irAE.

-A19-

IMPACT OF HOPE ON VERY OLD DCD (>70 YEARS) LIVERS: INSIGHTS FROM A BELGIAN BI-CENTREIC EXPERIENCE. M. Foguene (1), A. Dubois (1), J. Blondeel (2), L. Marique (1), A. Channaoui (1), O. Ciccarelli (1), L. Coubeau (1), G. Dahlqvist (3), K. Vandevoorde (2), K. Degezelle (2), I. Jochmans (2), M. Sainz Barriga (2), J. Pirenne (2), E. Bonaccorsi-Riani (1), D. Monbaliu (2) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Brussels, Belgium, Department of Abdominal Surgery and Transplantation, [2]

Introduction: Liver graft recipients from donors after circulatory death (DCD) face an increased risk of complications such as primary non-function and non-anastomotic biliary stricture (NAS). This is due to the warm ischemia time, inherent to the DCD procurement. Similarly, liver grafts from very old (>70 years) donors are known to increase these risks, although they represent a valuable option to safely increase the donor pool. Ex-situ end-ischemic hypothermic oxygenated perfusion (HOPE) of DCD-grafts <60 years has been demonstrated to reduce the incidence of complications following liver transplantation (LT).

Aim: Results of HOPE in grafts from very Old-DCD (>70 years) remains scarce. Therefore, we aim to study impact of HOPE on these specific grafts, from a bi-centric Belgian cohort.

Methods: Data from 95 LT using >70 years DCD-graft, transplanted in 2 Belgian centres (Leuven, Brussels) between 2015 and 2025 were collected. Of those, 53 were preserved with end-ischemic HOPE (Old-DCD-HOPE) while 42 were preserved in static cold storage (Old-DCD-SCS). Graft-threatening and graft-related complications were identified. Graft-threatening complications was defined as leading to recipient death or reLT. Graft-related complications were listed as: primary non function, NAS, anastomotic biliary stricture, biliary fistula, vascular complications (artery, portal vein and hepatic vein), need for renal replacement therapy after LT, relaparotomy within 10 days after LT and acute rejection.

Results: An increased proportion of DCD-graft >70 years were implanted since HOPE introduction. Recipient characteristics (indication, age, MELD score) were similar in both groups. Under HOPE, graft were perfused for 172 minutes on average. Previously, they were preserved statically in the cold for 216 minutes. Taken together, SCS and HOPE lasted on average for 388 minutes (=216+172 minutes). This was significantly longer than in Old-DCD-SCS group (332 minutes, $p=0.002$). Warm ischemia times were comparable between groups (42 vs. 41 minutes, $p=0.534$). Donors were older in the Old-DCD-HOPE compared to the Old-DCD-SCS (76.9 vs. 73.5 years old, $p<0.001$). Old-DCD-HOPE presented a lower rate of graft-related complications (0.57/patient) compared to Old-DCD-SCS (1.14/patient) ($p=0.003$), including NAS (5.7% vs 21.4%, $p=0.047$). Similarly, need for renal replacement therapy after LT was reduced in OLD-DCD-HOPE (3.8% vs. 16.7%, $p=0.075$). Furthermore, graft-threatening complications (leading to reLT or death) were reduced after HOPE perfusion (7.5% vs 28.6%, $p=0.015$). There was no difference in 1-year graft survival (84.0% vs. 76.0%, $p=0.238$). Follow-up was shorter in HOPE group (16.7 months) compared to Old-DCD-SCS group (24.1 months, $p=0.007$). This is due to the relative novelty of HOPE implantation as preserving strategy in LT (2022). Yet, average follow-up reached more than 1 year in Old-DCD-HOPE. This is considered as sufficiently long to detect any graft-related complication.

Conclusions: These findings support that using of HOPE for DCD-graft >70 years results with fewer graft-related and graft-threatening complications. By enabling the safe transplantation of grafts from very old DCD donors, HOPE contributes to a meaningful expansion of donor availability. Larger prospective studies are warranted to confirm these encouraging results.

-A20-

THE ALBI GRADE, A PROGNOSTIC MARKER IN ADVANCED CHRONIC LIVER DISEASE: A PROSPECTIVE SINGLE-CENTRE STUDY. E. Cailteux (1), M. De Callatay (1), A. Collard (2), G. Dahlqvist (1), Y. Horsmans (1), N. Lanthier (1), P. Starkel (1), B. Delire (3) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Hepato-gastroenterology, [2] UCL Saint-Luc, Brussels, Belgium, Statistics, [3] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Hepato-gastroenterology.

Introduction: The ALBI score is an index of liver function based solely on albumin and bilirubin levels. The ALBI grade is categorised on the basis of the ALBI score ranging from 1 to 3, with 1 being the best and 3 the worst. Until now, the ALBI grade has mainly been used in the field of hepatocellular carcinoma (HCC), where it has been validated as a reliable prognostic marker. Advanced hepatic fibrosis (AHF) is associated with significant morbidity and mortality. Retrospective studies suggest that the ALBI grade can also be used as a prognostic marker in AHF. To date, only one prospective study has analysed the ALBI score in patients with 'stable' decompensated cirrhosis, concluding that it was a better predictor of survival and complications than the Child-Pugh and MELD score.

Aim: The aim of this study is to prospectively evaluate the ALBI score/grade in AHF.

Methods: This prospective single-centre study included patients with AHF, excluding those with HCC. Advanced hepatic fibrosis was defined as Metavir stage F3 or F4, as determined by liver biopsy if available,

or by non-invasive elastometry (Fibroscan), or radiological, clinical, or laboratory evidence of cirrhosis. At inclusion, the Child-Pugh, MELD, and ALBI scores/grades were calculated. The primary objective was to assess, according to ALBI grade, the occurrence of death, all-cause hospitalisation, hospitalisation for hepatic decompensation (variceal haemorrhage, symptomatic ascites or hepatic encephalopathy), intensive care unit (ICU) admission and liver transplantation at one year. The secondary objective was to compare the ALBI score with other prognostic scores, such as the Child-Pugh and MELD scores.

Results: Between September 2023 and July 2024, a total of 162 patients were included in the study. The mean age was 60.7 years, 62.3% of them were male. The two main causes of AHF were alcohol use disorder and metabolic dysfunction-associated steatohepatitis. Of these patients, 95 had ALBI grade I (58.6%), 51 had ALBI grade II (31.5%), and 16 had ALBI grade III (9.9%). After a follow-up of one year, a total of twelve deaths (7.4%) were observed, with a significant difference according to ALBI grade (grade I: 2.1%; grade II: 13.7%; grade III: 18.8%; $p = 0.0036$). Hospitalisations for all causes were more frequent according to ALBI grade (I: 16.8%, II: 56.9%, III: 81.3%; $p < 0.0001$), as were hospitalisations for infections (I: 2.1%, II: 31.4%, III: 43.8%; $p < 0.0001$), symptomatic ascites (I: 3.2%, II: 13.7%, III: 43.8%; $p < 0.0001$) and hepatic encephalopathy (I: 4.2%, II: 21.6%, III: 43.8%; $p < 0.0001$). A higher proportion of patients with grade III were admitted to the ICU (grade I: 18.8%; grade II: 10.7%; grade III: 75%; $p = 0.0002$). Thirteen patients underwent transplantation: none in the grade I group; 5 (9.8%) in the grade II group; and 8 (50%) in the grade III group ($p < 0.0001$). The overall survival probability according to the Kaplan-Meier method, was lower in the ALBI grade III group than in the grade II and I groups ($p = 0.0021$). The probability of all-cause hospitalization or associated with liver decompensation events was significantly higher in group III compared to groups I and II ($p < 0.0001$ and $p < 0.0001$). The AUROC for overall survival and hepatic decompensation events for ALBI, Child-Pugh and MELD scores was 0.8136, 0.7950, 0.6839 and 0.8257, 0.8639, 0.8211 respectively. The comparison of dichotomized scores, according to the Contal & O'Quigley method, showed that ALBI grade was the strongest predictor of survival, with a chi-square of 39.63 ($p < 0.0001$), and of hepatic decompensation with a chi-square of 69.66 ($p < 0.0001$). In multivariate analysis, sodium level and active alcohol misuse were two main variables associated to the death while the bilirubin and albumin levels, and the platelets counts were associated to liver decompensation events.

Conclusions: Our study, which is the first prospective study on ALBI score in AHF, highlights the ALBI score as a superior predictor of overall survival and liver decompensation events in ALF, outperforming MELD and Child-Pugh scores. ALBI demonstrates the highest discriminative ability for risk stratification and differentiating survival profiles and the occurrence of hepatic decompensation in our cohort. It supports its routine use in clinical practice.

-A21-

ISOLATED IGG ELEVATION IN PATIENTS WITH PERSISTENTLY NORMAL TRANSAMINASES DOES NOT AFFECT THE OUTCOME OF AUTOIMMUNE HEPATITIS: OR JUST A LITTLE BIT? L. Grossar (1), S. Raevens (2), C. Van Steenkiste (3), I. Colle (4), C. De Vloo (5), H. Orlent (6), J. Schouten (7), M. Gallant (8), A. Van Driessche (9), S. Lefere (10), L. Devisscher (11), A. Geerts (2), H. Van Vlierberghe (2), X. Verhelst (2) / [1] Ghent University Hospital, Ghent, Belgium, Internal Medicine and Paediatrics, [2] Ghent University Hospital, Ghent, Belgium, Gent, Belgium, Gastroenterology and Hepatology, [3] AZ Maria Middelaes, Ghent, Belgium, Gastroenterology and Hepatology, [4] AZORG AALST, Aalst, Belgium, Gastroenterology and Hepatology, [5] AZ Delta, Belgium, Gastroenterology and Hepatology, [6] AZ Sint-Jan Brugge, Brugge, Belgium, Gastroenterology and Hepatology, [7] NETwerk, VITAZ Sint-Niklaas/UZA, Edegem, Belgium, Gastroenterology and Hepatology, [8] Jan Yperman Hospital, Ieper, Belgium, Gastroenterology and Hepatology, [9] AZ Glorieux Ronse, Ronse, Belgium, Gastroenterology and Hepatology, [10] Ghent University, Ghent, Belgium, Liver Research Centre Ghent, [11] Ghent University, Ghent, Belgium, Gastroenterology and Hepatology.

Introduction: In autoimmune hepatitis (AIH), follow-up of disease activity after induction treatment mainly relies on normalization of transaminases (TA) and immunoglobulin G (IgG). The international autoimmune hepatitis group consensus criteria defined complete biochemical response as normalization of TA and IgG within six months after induction treatment. This intermediate endpoint correlated with superior liver-related survival. The association of IgG with survival outcomes is more contested than TA normalization, illustrated by studies reporting a stronger and independent association between these outcomes and TA normalization at six months, compared with IgG. Furthermore, a subset-analysis from a recent multicentre Spanish and German cohort described no significant difference in cirrhosis

development between subjects with AIH after persistent TA normalization, according to their IgG evolution. **Aim:** We aimed to perform a subset-analysis in our own previously described cohort to investigate whether IgG evolution after sustained TA normalization influenced development of cirrhosis during follow-up. **Methods:** We performed an additional analysis from our own retrospective, real-world, multicentre cohort of subjects with AIH and identified those with persistently normal TA, and without cirrhosis at initial diagnosis. Next, all recorded IgG levels were collected allowing classification of subjects with either persistently normal IgG (IgGn), fluctuating IgG (IgGf), or persistently elevated IgG (IgGe). Development of cirrhosis was defined by suggestive clinical, laboratory and imaging findings, and/or METAVIR F4 stage in follow-up biopsy.

Results: From an initial cohort of 213 subjects with AIH, 95 with persistently normal TA and without cirrhosis could be identified. According to IgG evolution, 76 out of 95 (80.0%) had persistently normal IgG, whereas 17 (17.9%) and 2 (2.1%) could be classified as IgGf and IgGe, respectively. During a median follow-up of 8.1 years (interquartile range: 1.2 – 15.1 years), seven (7.4%) subjects developed cirrhosis. When comparing proportions according to IgG evolution, the proportion of subjects with persistently normal IgG who developed cirrhosis was significantly lower than the proportion with either persistently elevated or fluctuating IgG: 3/76 (4.0%) versus 1/2 (50%) and 3/17 (17.6%), respectively (Fisher's exact test p-value for differences in proportions between IgGn, IgGf, and IgGe = 0.01635). When comparing persistently normal IgG with fluctuating IgG and persistently IgG together as one group, occurrence of cirrhosis remained significantly less frequent in the subgroup with persistently normal IgG: 4.0% versus 21.1% respectively (Fisher's exact test p-value = 0.02785).

Conclusions: In our subset-analysis, development of cirrhosis occurred significantly less frequent in subjects with persistently normal TA and IgG, to those with abnormal IgG during follow-up. These findings are in contrast with a recent multicentre cohort, and further emphasize the importance of large datasets with long-term follow-up, especially when the incidence of the outcome of interest is low.

-A22-

THE IMPACT OF PRIOR BARIATRIC SURGERY ON PATIENTS WITH COMPENSATED AND DECOMPENSATED ALCOHOL-RELATED LIVER DISEASE: RESULTS OF AN OBSERVATIONAL MULTICENTRE STUDY. A. Marot (1), J. Bitton (2), S. Belhoussine Drissi (2), L. Weichselbaum (2), D. Degré (2), O. Borgniet (3), M. Van Hoof (4), E. Trépo (2), T. Gustot (2), H. Njimi (5), P. Deltenre (4), C. Moreno (2) / [1] CHU UCL Namur, Yvoir, Belgium, Gastroenterology and Hepatology, [2] Hôpitaux Universitaires de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, Université Libre de Bruxelles, Brussels, Belgium, [3] CHU UCL Namur, Yvoir, Belgium, Department of Gastroenterology and Hepatology, [4] Clinique Saint-Luc Bouge, Namur, Belgium, Department of Gastroenterology and Hepatology, [5] Hôpitaux Universitaires de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Belgium, Biomedical statistics, Université Libre de Bruxelles, Brussels, Belgium.

Introduction: Bariatric surgery (BS) is the most effective treatment for achieving long-term weight loss in patients with severe obesity and associated metabolic conditions. Recent data suggest an increased risk of alcohol-related liver disease (ARLD) in patients with prior BS. The impact of prior BS on the course of patients with ARLD is unclear.

Aim: The main aims of this study were: 1) to evaluate the impact of a prior BS on liver-related outcomes in patients with ARLD at different stages of severity (i.e. compensated ARLD, decompensated ARLD, and alcohol-associated hepatitis [AAH]), and 2) to assess the risk of hepatic decompensation in patients with compensated ARLD both with and without a prior BS in a large multicentre retrospective study.

Methods: We included 794 patients with ARLD in three Belgian centres (HUB Erasme Hospital, Saint-Luc Bouge and CHU UCL Namur) between January 4th 2010 and 31st December 2024. The median follow-up after inclusion was 2.6 (IQR: 0.4 – 6.8) years. Cumulative incidence functions were applied to estimate the risk of death in patients with AAH and those with compensated and decompensated ARLD separately. A competing-risks regression procedure was performed to identify variables associated with death, taking into account liver transplantation as competing risk. A similar analysis was performed in compensated ARLD patients to identify variables associated with hepatic decompensation.

Results: Almost 15% of patients (115/794) with ARLD had a prior BS, of whom 81 (70%) had undergone Roux-en-Y gastric bypass. At inclusion, 377 patients (47.5%) had a compensated ARLD, 189 patients (23.8%) had a decompensated ARLD, and 228 patients (28.7%) had an AAH. Compared to the non-BS

group, patients with a prior BS were predominantly female (50.4% vs. 27.5%, $p < 0.001$) and younger (51 vs. 56 years, $p < 0.001$). They presented with more severe disease, i.e. with a higher frequency of ascites (54% vs. 39.5%, $p = 0.003$), lower albumin levels (30.4 g/L vs. 34.9 g/L, $p < 0.001$) and a trend toward more frequently hepatic encephalopathy (27.8% vs. 20.1%, $p = 0.057$). Compared to the non-BS group, the proportion of Child-Pugh C was higher in the BS group (47.4% vs. 27.4%, $p < 0.001$) as well as the proportion of MELD score > 20 (31.3% vs. 20.2%, $p = 0.008$). Compared to the non-BS group, patients with a prior BS were also younger at time of transplantation (48 vs 58 years, $p < 0.001$) and at death (50 vs 59 years, $p < 0.001$). The rate of liver transplantation was similar between the two groups. In patients with AAH, cumulative incidence of death at 6 months was not different between the BS and the non-BS group (33.9% vs 47.4%, $p = 0.10$). In multivariable analyses, age (SHR: 1.03, 95% CI: 1.01 – 1.05, $p = 0.001$) and MELD score at baseline (SHR: 1.08, 95% CI: 1.05 – 1.11, $p < 0.001$) were independently associated with mortality, but not prior BS (SHR: 0.57, 95% CI: 0.29 – 1.11, $p = 0.10$). In patients with compensated and decompensated ARLD, cumulative incidence of death at 3 years was not different between the BS and the non-BS group (23.1% vs 21.5%, $p = 0.77$). In multivariable analyses, MELD score at baseline (SHR: 1.19, 95% CI: 1.14 – 1.23, $p < 0.001$), abstinence (SHR: 0.31, 95% CI: 0.13 – 0.75, $p = 0.01$), and prior BS (SHR = 5.98, 95% CI: 1.87 – 19.1, $p = 0.03$) were independently associated with mortality. In the subgroup of patients with compensated ARLD, hepatic decompensation was more frequent in the BS group compared to the non-BS group (84.2% vs 25.0%, $p = 0.01$). In multivariable analyses, MELD score at baseline (SHR: 1.12, 95% CI: 1.05 – 1.19, $p < 0.001$) and prior BS (SHR: 2.24, 95% CI: 1.16 – 4.43, $p = 0.02$) were independently associated with first hepatic decompensation.

Conclusions: Despite being younger at the time of inclusion, liver transplantation and death, ARLD patients with a prior BS have more severe liver disease than those with no prior BS. Multivariable analyses show that prior BS is associated with higher mortality in patients with compensated and decompensated ARLD, but not in patients with AAH. In patients with compensated ARLD, prior BS is also associated with a higher risk of first hepatic decompensation.

-A23-

ASSESSMENT OF SPLENIC ELASTICITY IN PATIENTS WITH ADVANCED CHRONIC LIVER DISEASE: A RETROSPECTIVE MONOCENTRIC STUDY. A. Lorge (1), S. André-Dumont (1), G. Dahlqvist (1), B. Delire (1), Y. Horsmans (1), P. Stärkel (1), N. LANTHIER (2) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'Hépatogastroentérologie, [2] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Service d'Hépatogastroentérologie.

Introduction: Spleen stiffness measurement (SSM) is a non-invasive screening tool proposed to assess significant portal hypertension. SSM cut-offs have been proposed by Baveno VII for patients with compensated advanced chronic liver disease (cACLD): group 1 (rule-out zone) with a SSM < 21 kPa, group 2 (grey-zone) with a SSM between 21 and 50 kPa and group 3 (rule-in zone) with a SSM > 50 kPa.

Aim: Given the relative novelty of this technique, our aim is to assess the number of patients in each of these groups and their clinical characteristics, particularly regarding the complications of cirrhosis, and to correlate these findings to the hepatic venous pressure gradient (HVPG) measurement.

Methods: Adult patients with available SSM were retrospectively included at our single centre between August 2023 and June 2025. Patients without cACLD (liver stiffness measurement (LSM) < 10 kPa), with cardiac hepatopathy or history of liver transplantation were excluded. SSM and LSM were measured with the 110 and 50 Hz modules respectively on the same day by vibration-controlled transient elastography using the FibroScan 630 Expert®. Baseline clinical and biological data of patients were collected at the time of the SSM. Baveno VII cut-offs were used to divide patients into three groups based on the values of the SSM.

Results: 161 patients were included, with a median age of 60 years (interquartile, IQR 48 - 67), mainly men for 66% and with a median body mass index of 27.2 kg/m² (IQR 24.5 - 31.2). The causes of cACLD and cirrhosis were as follows: alcohol-related liver disease (39%), metabolic dysfunction-associated steatotic liver disease (32.5%), hepatitis C virus (10.0%), auto-immune hepatitis (3.7%), primary biliary cholangitis (3.1%), hepatitis B virus (3.1%) and others (8.6%). SSM was successfully measured, with an average of 12 valid measurements and an average IQR range of 11.7 kPa. Based on SSM cut-offs proposed by Baveno VII, only 3 patients were classified in group 1 (mean SSM 12.9 kPa, IQR 9.1-14.3), 75 in group 2 (mean SSM 37.3 kPa, IQR 32-42.4) and 83 in group 3 (mean SSM 71.9 kPa, IQR 55.9-83.5). Liver elasticity significantly differed between group 3 (median 29.5kPa) and groups 1 and 2 (14.7 and 21.7 kPa

respectively, $p < 0.001$). LSM and SSM values were correlated ($r = 0.43$, $p < 0.001$). Groups 2 and 3 were also different in terms of platelet count (151 vs $115 \times 10^3/\text{mL}$, $p < 0.001$), total bilirubin levels (0.7 vs 0.9 mg/dL, $p = 0.03$), albumin levels (44 vs 41 g/L, $p = 0.004$), white blood cell count (5.3 vs $6.9 \times 10^3/\mu\text{L}$, $p = 0.003$), C-reactive protein (1.6 vs 3.0 mg/L, $p = 0.005$) and Model for End Stage Liver Disease (MELD) score (9 vs 10 , $p = 0.02$). Those two groups also differed in terms of HVPg measurement (9.5 - $n = 22$ - vs 12.0 mmHg - $n = 29$ -, $p = 0.01$), spleen size (11.3 vs 13.0 cm, $p < 0.001$), history of ascites (15 vs 30% , $p = 0.039$), presence of esophageal varices (32 vs 53% , $p = 0.006$) but not in terms of history of variceal bleeding (4 vs 11% , $p = 0.32$). No patients in group 2 were taking beta-blockers, whereas 15 patients (18%) in group 3 were ($p < 0.001$). In the subgroup of patients with HVPg measurement ($n = 51$), there was a good correlation between LSM and HVPg values ($r = 0.49$, $p < 0.001$) but not between SSM and HVPg values ($r = 0.26$, $p = 0.064$).

Conclusions: Less than 2% of patients with cACLD or cirrhosis fall within the range that allows portal hypertension to be ruled out (group 1) based on the cut-offs proposed by Baveno VII. Patients in the grey zone (group 2) and the rule-in zone (group 3) differ according to biological markers of liver function. Patients in the rule-in zone also have a higher prevalence of ascites but not of variceal bleeding. Surprisingly, HVPg correlates more strongly with hepatic elasticity than splenic elasticity. The Baveno VII algorithm and cut-offs can therefore be considered as indicators but should be re-evaluated before their clinical utility can be confirmed in patients with cACLD and cirrhosis. The longitudinal evolution of splenic elasticity and long-term follow-up will also be important to assess.

-A24-

INTRAOPERATIVE AND EARLY POSTOPERATIVE MORTALITY AFTER LIVER TRANSPLANTATION: INSIGHTS FROM 27 YEARS OF EXPERIENCE IN A HIGH-VOLUME TERTIARY CENTRE. H. Vaesen Bentein (1), I. Niesten (1), V. De Pauw (2), C. Evers (3), C. Verslype (4), H. van Malenstein (4), W. Laleman (4), S. Van der Merwe (4), J. Verbeek (4), M. Sainz Barriga (3), D. Monbaliu (3), J. Pirenne (3) / [1] KU Leuven, Leuven, Belgium, Faculty of Medicine, [2] University Hospital Brussels, Vrije Universiteit Brussel, Belgium, Department of Thoracic Surgery, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Abdominal Transplant Surgery, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Intraoperative and early postoperative mortality following liver transplantation (LT) are rare but devastating events that profoundly affect both patients' families and multidisciplinary transplant teams. As most existing studies focus on long-term outcomes, early mortality remains underreported and poorly characterized. A better understanding of these critical events is essential to optimize perioperative management, guide medical and surgical decision-making and improve overall survival.

Aim: This study aims to address this knowledge gap by providing a detailed analysis of intraoperative and first-week mortality following LT in a high-volume tertiary centre. We sought to describe the incidence, causes and determinants of these early deaths and to identify donor, recipient and perioperative factors contributing to their occurrence.

Methods: We conducted a retrospective single-centre observational study of the adult LT procedures performed at University Hospitals Leuven between January 1997 and May 2024. Patients who had undergone living donor, split-liver or multi-organ transplantations were excluded. Descriptive analyses were performed to characterize the patients who died within the first postoperative week, with particular attention to intraoperative and 24-hour mortality. To explore risk factors associated with first-week mortality, propensity score-matched (PSM) and inverse probability of treatment-weighted (IPTW) cohorts were constructed to compare early deaths with longer-term survivors. Both models included donor, recipient and operative variables such as age, body mass index, MELD and UNOS scores, cold ischemia time, surgical time and transfusion requirements.

Results: A total of 1,693 LT recipients were included. The incidence of intraoperative mortality was 0.53% ($n=9$) and the overall first-week mortality was 1.36% ($n=23$). The leading causes of intraoperative death were haemorrhage ($n=2$), cardiogenic shock ($n=2$), and thrombotic events ($n=2$). Among patients who died within the first postoperative week, the most common causes were haemorrhage ($n=5$), cardiogenic shock ($n=4$), septic shock ($n=3$), and thrombotic events ($n=3$). Comprehensive risk analysis using PSM and IPTW approaches revealed that only donor age and surgical duration were significantly associated with early mortality. These observations were consistent across analytical methods, but require confirmation in larger, multicentre cohorts.

Conclusions: This study provides a comprehensive overview of intraoperative and first-week mortality

following LT at a high-volume tertiary centre over nearly three decades. While such events are rare, multifactorial, and therefore challenging to predict, our findings underscore the importance and need for refined preoperative risk stratification, vigilant monitoring and rapid, targeted, multidisciplinary interventions to further reduce mortality after LT transplantation.

-A25-

THE EFFECT OF GLP-1 ANALOGUES ON LIVER STEATOSIS AND FIBROSIS IN DIABETIC AND OBESE PATIENTS IN A CLINICAL SETTING. Y. Polspoel (1), S. François (2), H. Reynaert (2), H. Degroote (2) / [1] UZ Brussel, Brussels, Belgium, Internal Medicine, [2] UZ Brussel, Brussels, Belgium, Gastro-Enterologie.

Introduction: Metabolic dysfunction–associated steatotic liver disease (MASLD) has become the most prevalent hepatic disease worldwide. It is strongly associated with type 2 diabetes mellitus (T2DM) and obesity, which share an intertwined pathophysiology driven by insulin resistance, hyperinsulinemia, and subsequent dysregulation of lipid and glucose metabolism. These conditions represent key components of the metabolic syndrome, a growing global health burden linked to substantial morbidity and mortality. Given this close relationship, therapeutic strategies that improve insulin sensitivity and promote weight loss may also benefit hepatic outcomes. Glucagon-like peptide-1 receptor agonists (GLP1a) have demonstrated impressive effects on weight reduction and glycemic control. Emerging evidence further suggests that GLP1a therapy may improve hepatic steatosis and possibly fibrosis. However, most available data arise from controlled a limited amount of clinical trials with limited generalizability to routine practice.

Aim: This study aimed to evaluate the real-world effects of GLP1a therapy on hepatic steatosis and fibrosis in diabetic and obese patients with MASLD, treated at the diabetes clinic of UZ Brussel.

Methods: A non-interventional observational study was conducted at the diabetes clinic of UZ Brussel. Adult patients with obesity and/or T2DM and non-invasively confirmed MASLD were included if they were initiating- or had been on GLP1a therapy for at least 12 months. Markers of hepatic damage (AST, ALT, GGT), steatosis (Fatty Liver Index), and fibrosis (FIB-4 index, APRI score, NAFLD Fibrosis Score) were assessed at baseline and after 12 months. Secondary outcomes included weight, BMI, waist circumference, HbA1c, fasting glucose, and lipid profile. Data were analysed using paired t-tests or Wilcoxon signed-rank tests, depending on distribution.

Results: 48 patients were included, all with T2DM, obesity, and liver steatosis at baseline. No statistically significant changes in AST, ALT, or GGT were observed, although a downward trend was noted, particularly in subjects with elevated baseline levels. A significant reduction of the Fatty Liver Index, and thus liver steatosis, was observed. While fibrosis indices showed favourable, but non-significant, downward trends. Significant improvements were recorded in weight, BMI, waist circumference, HbA1c, fasting glucose, and HDL cholesterol. These findings suggest that GLP1a therapy may contribute to the improvement of hepatic steatosis in patients with MASLD, alongside its other established metabolic benefits. Although statistically significant improvements in non-invasive fibrosis markers were not observed within the 12-month period, the consistent downward trends may reflect the early stages of a longer term therapeutic response. Compared to controlled clinical trials, the magnitude of change observed in this study was modest, likely due to the inherent challenges of a real-world clinical setting, where factors such as adherence, adverse events, polypharmacy, and variable levels of medical literacy play a significant role. Nevertheless, even within this complex environment, GLP1a therapy demonstrated measurable clinical benefits, particularly in reducing liver steatosis and improving glycemic- and weight-control.

Conclusions: In a real-world clinical setting, GLP1a therapy was associated with significant improvements in hepatic steatosis and metabolic parameters in patients with MASLD.

-A26-

DIETARY INTAKE AND LIFESTYLE HABITS IN PATIENTS WITH STEATOTIC LIVER DISEASE: A CROSS-SECTIONAL STUDY. S. Declerck (1), G. Henin (1), S. André-Dumont (1), A. Goffaux (1), P. Baldin (2), P. Henry (3), A. Gouw (4), C. Sampoux (5), A. Loumaye (6), P. Stärkel (1), N. Lanthier (1) / [1] UCLouvain, Cliniques universitaires Saint-Luc, Belgium, Hépatogastroentérologie, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Brussels, Belgium, Pathology, [3] Institute of pathology and genetics, Gosselies, Belgium, Charleroi, Belgium, Pathology, [4] University Medical Centre Groningen, Groningen, The Netherlands, Pathology and medical biology, [5] Lausanne University Hospital (CHUV),

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Introduction: Unhealthy dietary patterns and insufficient physical activity are well-established contributors to the development of metabolic-associated steatotic liver disease (MASLD). More recently, the consumption of ultra-processed foods (UPF) has emerged as a major nutritional concern, being linked to an increased risk of MASLD. However, data remain limited regarding the detailed characterization of dietary intake and physical activity in patients with alcohol-related liver disease (ALD) and, more broadly, in patients with steatotic liver disease (SLD).

Aim: The primary aim of this study was to identify and compare dietary habits, including UPF consumption, and physical activity levels in patients with SLD versus healthy controls. The secondary aim was to evaluate the association between UPF intake and histologically assessed liver disease severity.

Methods: A total of 247 patients with SLD and 31 healthy controls were prospectively recruited. Dietary intake and UPF consumption were assessed using a 24-hour dietary recall. Food processing level was classified according to the NOVA system, and nutrient intake quantified in % of the total energy intake (TEI) and grams using the Nubelpro software. Physical activity was evaluated using the International Physical Activity Questionnaire (IPAQ). Hepatic steatosis and fibrosis were quantified by vibration-controlled transient elastography (VCTE). A subset of patients with clinically suspected advanced disease underwent liver biopsy for histopathological evaluation.

Results: Among the 247 patients with SLD, 152 had MASLD and 95 had ALD. The biopsy subgroup included 94 patients (54 MASLD, 40 ALD). As expected, patients with MASLD compared to patients with ALD and controls, exhibited significantly higher BMI (32 vs 26 vs 22 kg/m², $p < 0.0001$), waist circumference (112 vs 100 vs 79 cm, $p < 0.0001$), and HOMA-IR values (4.1 vs 2.0 vs 1.0, $p < 0.0001$). Type 2 diabetes was common in MASLD (41%), uncommon in ALD (5%), and absent in controls. Conversely, patients with ALD compared to MASLD patients displayed higher alanine aminotransferase (69 vs 47 U/L, $p < 0.0001$), and gamma-glutamyl transferase (156 vs 44 U/L, $p < 0.0001$) levels. Liver stiffness measurement and controlled attenuation parameter values were elevated in both MASLD and ALD groups compared with controls (11 vs 12 vs 4 kPa $p = 0.0004$; 328 vs 299 vs 196 dB/m, $p < 0.0001$). Nutritional analysis showed that ALD patients consumed more total calories than MASLD patients (2290 vs 1620 kcal, $p < 0.0001$), despite having a lower BMI, mainly due to higher alcohol intake. When expressed as percentage of TEI%, ALD patients compared to MASLD patients and controls consumed fewer proteins, lipids, carbohydrates, and dietary fibres (proteins: 11 vs 17 vs 16 %TEI, $p < 0.0001$; lipids: 23 vs 37 vs 42 %TEI, $p < 0.0001$; carbohydrates: 27 vs 42 vs 37 %TEI, $p < 0.0001$; fibres: 0.8 vs 1.9 vs 2.4 %TEI, $p < 0.0001$). In MASLD, macronutrient distribution was similar to controls, except for a lower fibre intake (16 vs 23 g/day, $p < 0.0001$). Interestingly, in the biopsied MASLD subgroup, significant fibrosis ($F \geq 2$) was associated with lower fibre consumption ($F < 2$: 19 vs $F \geq 2$: 15 g/day, $p = 0.0259$). Regarding UPF intake, ALD patients consumed markedly higher amounts of processed foods (NOVA 3) than both MASLD patients and controls (54 vs 27 vs 30 %TEI, $p < 0.0001$), largely attributable to alcohol consumption. No significant differences in NOVA categories 1–4 were observed between MASLD patients and controls. Histologically, UPF consumption was not associated with the severity of the liver disease in terms of steatosis, activity, or fibrosis in either MASLD or ALD patients. Finally, for physical activity, the total physical activity (MET-min/week) was higher in controls compared to patients with ALD (3013 vs 1533 MET-min/week, $p < 0.0386$). Controls dedicated a larger proportion of their activity to leisure-time exercise (54% vs. 11% in MASLD and 17% in ALD, $p < 0.0001$).

Conclusions: We demonstrated that patients with SLD exhibit lower fibre intake, and reduced leisure-time physical activity compared with healthy controls. Importantly, a low fibre intake, but not UPF consumption, was linked to fibrosis severity in patients with MASLD, suggesting that specific nutrient components may be more relevant than global UPF exposure. These findings support the value of targeting physical activity and emphasize the importance of dietary fibre as a potentially modifiable factor in SLD.

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DEVELOPMENT AND CONTENT VALIDATION OF A SYMPTOM BURDEN SCALE FOR LIVER CIRRHOSIS. L. Seynhaeve (1), T. Penninck (2), C. De Vloo (3), S. De Meulder (3), J. Dewyspelaere (3), K. Ferdinande (4), L. Harlet (3), J. Decaestecker (3), L. Kinnaer (5) / [1] AZ Delta, Roeselare, Belgium, Department of Hepatology, Rumbeke, Belgium, [2] Ghent University, Ghent, Belgium, Master in Science in Nursing and Midwifery, Faculty of Medicine and Health Sciences, Ghent University, Ghent, Belgium, [3] AZ Delta, Belgium, Department of Gastroenterology and Hepatology, Rumbeke, Belgium, [4] Ghent University,

Introduction: Liver cirrhosis is a progressive condition in which healthy liver tissue is replaced by fibrosis, representing a major global health burden and accounting for nearly 2% of deaths in Europe (1). Cirrhosis results from various chronic liver diseases including alcohol use disorder, viral hepatitis and MASLD, and may progress from a compensated to a decompensated stage with a significant decline in survival (2-3). Patients experience a substantial and heterogeneous symptom burden that significantly impairs their quality of life (4). Although several generic instruments and liver disease questionnaires are available (5-6), none comprehensively capture the multidimensional symptom burden and personal experiences unique to patients with liver cirrhosis. Consequently, there is a need for a validated, patient-centred tool that reflects the complexity of this condition and can be applied in both clinical practice and research settings.

Aim: This study aims to develop a symptom burden instrument specifically tailored to patients with liver cirrhosis and to evaluate its content validity.

Methods: A rapid review was conducted to identify the most frequently reported symptoms in patients with liver cirrhosis, which were grouped into three initial domains: physical, psychological and social symptoms. A hepatologist, a clinical nurse specialist and an expert in patient education were involved throughout the process to ensure the clinical relevance. The preliminary instrument consisted of 35 items. Content validity was evaluated through a two-round Delphi study involving healthcare professionals and patients with liver cirrhosis. Participants rated the relevance, clarity and feasibility of each item on a 5 Point Likert Scale. Participants could also give qualitative feedback on clarity and missing elements. The Item-Content Validity Index (I-CVI; cut-off ≥ 0.78) and Scale-Content Validity Index (S-CVI; cut-off ≥ 0.90) were calculated to quantify agreement (7).

Results: After two Delphi rounds, 24 items met the predefined threshold for content validity I-CVI ≥ 0.78 , resulting in a tool structured across four domains: physical, psychological, social and treatment adherence. The final S-CVI was 0.89 for healthcare professionals and 0.85 for patients. Qualitative feedback led to refinements in content, item formulation, response options and the removal of redundant questions.

Conclusions: We developed a symptom burden instrument specifically designed for patients with liver cirrhosis. The tool demonstrates good content validity and has the potential to serve as a patient-centred measure for systematic symptom assessment. Its implementation in clinical practice may improve symptom recognition, guide individualized care and enhance shared decision-making. Further psychometric testing in larger patient populations is warranted to confirm reliability and construct validity.

-A28-

CEROID-LADEN MACROPHAGES AS HISTOLOGICAL BIOMARKERS IN METABOLIC DYSFUNCTION ASSOCIATED STEATOTIC LIVER DISEASE. A. Shangin (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Pathology.

Introduction: Ceroid-laden macrophages, characterised by cytoplasmic lipid-like pigment deposits, are observed in metabolic dysfunction-associated steatotic liver disease (MASLD) but their clinical significance remains underexplored.

Aim: This study investigates their role as histological biomarkers, evaluating correlations with disease activity and fibrosis in MASLD and metabolic dysfunction-associated steatohepatitis (MASH).

Methods: Liver biopsies from 54 patients (2004–2025) with suspected MASLD were examined and classified using the fatty liver inhibition of progression (FLIP) algorithm and steatosis, activity, and fibrosis (SAF) scoring. Ceroid-laden macrophages were identified via periodic acid-Schiff (PAS) staining with α -amylase digestion (highlighting granular cytoplasmic pigment) and graded (0–2) in parenchymal and portal compartments. Nonparametric tests assessed associations with disease activity (lobular inflammation, ballooning) and fibrosis.

Results: Parenchymal ceroid-laden macrophage grades were significantly higher in MASH (n=41) vs. MASLD (n=13; $p < 0.001$). Stratification showed lower macrophage grades in ‘burned-out’ cirrhosis compared to active cirrhosis ($p = 0.043$). Parenchymal ceroid-laden macrophage grades strongly correlated with disease activity ($r = 0.684$, $p < 0.001$). Portal macrophages exhibited a weaker but significant correlation with disease activity ($r = 0.281$, $p = 0.04$). Fibrosis analysis revealed a biphasic parenchymal pattern (peak at F2-F3, decline in F4; $p = 0.005$), while portal macrophages accumulated monotonically ($r = 0.551$, $p < 0.001$).

Conclusions: Ceroid-laden macrophages serve as compartment-specific biomarkers in MASLD: parenchymal burden reflects inflammatory activity and exhibits a distinct non-monotonic relationship with fibrosis,

peaking at intermediate stages (F2–F3) and declining sharply in cirrhosis (F4). The decline in parenchymal macrophages alongside sustained portal accumulation suggests a potential migration to portal tracts during disease progression. Their dynamic redistribution underscores spatially distinct roles in MASLD pathogenesis, offering insights for prognostic stratification and mechanistic studies.

-A29-

AUTO-IMMUNE HEPATITIS FOLLOWING COVID-19 VACCINATION AND SARS-COV2 INFECTION: A NARRATIVE REVIEW. M. Bendoumou (1), P. Langlet (2), T. Gustot (3) / [1] Université Libre de Bruxelles Faculté de Médecine, Brussels, Belgium, Internal Medicine, [2] Chirec Delta, Auderghem, Belgium, Gastroenterology, [3] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology and hepatology.

Introduction: Since the onset of the COVID-19 pandemic, both SARS-CoV-2 infection and vaccination have been implicated as potential triggers for de novo autoimmune hepatitis (AIH). **Aim:** This review summarizes published cases, outlining clinical and biological features, treatment approaches, and outcomes.

Methods: A PubMed search identified reports of new-onset AIH following SARS-CoV-2 infection or COVID-19 vaccination up to February 1, 2025. Inclusion criteria encompassed case reports, series, and reviews. Data were extracted on demographics, vaccine type, onset timing, laboratory findings, histology, treatments, and outcomes.

Results: A total of 74 post-vaccination AIH cases and 22 post-infection cases were included. Post-vaccination AIH predominantly affected older women (median age 62) and occurred mainly after mRNA vaccines, with a median onset of 14 days. Most patients showed marked transaminase elevation, high IgG, and positive ANA (74.3%). Liver biopsies (performed in 92% of cases) showed features compatible with AIH. A total of 80% of the 50 cases of our study with available serology and liver histology were classified as probable / definite AIH, according to the simplified AIH score. Corticosteroid therapy was effective in most cases (survival 95.9). Post-infection AIH cases showed similar features but affected younger individuals (median age 47), with uniformly favorable responses to immunosuppression.

Conclusions: New-onset AIH can occur following both SARS-CoV-2 infection or vaccination. Although these events remain rare, recognition of this association is essential for timely diagnosis and management.

-A30-

A CROSS-SECTIONAL STUDY CORRELATING BLOOD AMMONIA LEVELS AND ESOPHAGEAL VARICES IN LIVER CIRRHOSIS PATIENTS. D. Bharathi Shivananda (1), D. Reddy (1), K. Reddy (1), A. Thomas Benoy (1), A. Hatti (1), A. Aiyappa (1), M Parvathi (1) / [1] Bangalore Medical College and Research Institute, Bengaluru, India, Internal Medicine.

Introduction: Cirrhosis is characterized by progressive hepatic fibrosis and loss of functional hepatocyte mass, culminating in impaired liver function and clinically significant portal hypertension. The resulting portosystemic shunting further contributes to elevated systemic ammonia levels. Given the morbidity associated with oesophageal varices, there is a critical need for reliable, non-invasive markers that can predict their presence and guide timely endoscopic evaluation. This study systematically assessed serum ammonia concentrations, platelet count, portal vein diameter and flow velocity, international normalized ratio (INR), and spleen longitudinal diameter as potential non-invasive predictors of oesophageal varices in patients with cirrhosis.

Aim: The study was designed with two principal aims: first, to quantify systemic ammonia levels in patients with established liver cirrhosis, and second, to delineate their association with the endoscopic detection of oesophageal varices. As secondary aims, the study sought to characterize the relationship between ultrasonographic indicators of portal hypertension and the presence of varices, and to identify the clinical, biochemical, and sonographic determinants of variceal size in this population. Together, these objectives form the basis for evaluating a non-invasive predictive framework that may refine risk stratification and optimize timing of endoscopic surveillance in cirrhosis.

Methods: A comprehensive clinical evaluation, including demographic profiling, detailed medical history, and physical examination, was undertaken or obtained from existing medical records. Following informed consent, all patients underwent routine laboratory investigations, pelvic abdominal

ultrasonography, and assessment of hepatic reserve using the Child Pugh score. Peripheral blood samples were collected for standard biochemical analyses as well as targeted testing for autoimmune liver disease, hemochromatosis, Wilson's disease, and measurement of serum ammonia levels. Upper gastrointestinal endoscopy was performed, when clinically indicated, to identify and grade oesophageal varices. **Results:** Seventy patients with cirrhosis (mean age 43.7 ± 11.3 years; male-to-female ratio 5.36:1) were enrolled. Oesophageal varices (EV) were identified in 49 patients (70%), of whom 30 had small and 19 had large varices. Alcoholic liver disease was the predominant aetiology (74.3%). Serum ammonia levels were significantly higher in patients with EV compared to those without (139.2 ± 54.6 vs 108.0 ± 46.5 $\mu\text{mol/L}$; $p = 0.025$) and demonstrated a stepwise rise with increasing variceal size ($p < 0.001$). Patients with large EV had significantly lower platelet counts, higher INR, larger portal vein diameter, and reduced portal vein velocity (all $p < 0.05$). ROC analysis identified serum ammonia as the strongest non-invasive predictor of large EV (AUC 0.789), with an optimized cut-off >121.5 $\mu\text{mol/L}$ (89.5% sensitivity, 62.7% specificity). Platelet count and portal vein velocity showed moderate discriminatory ability for predicting absence of large EV. Multivariate regression revealed serum ammonia, platelet count, and portal vein diameter as independent predictors of variceal size.

Conclusions: Serum ammonia demonstrates strong discriminatory value for predicting the presence and size of oesophageal varices and outperforms other non-invasive markers. Platelet count and portal vein diameter also independently contribute to variceal risk stratification. These findings support the incorporation of serum ammonia, along with key biochemical and ultrasonographic parameters, into non-invasive prediction models to optimize early detection and guide the need for endoscopic surveillance in patients with cirrhosis.

-A31-

HEPATITIS C-RELATED CIRRHOSIS: PREDICTIVE FACTORS OF HEPATIC RECOMPENSATION AFTER SUSTAINED VIROLOGIC RESPONSE. R. Rejeb (1), A. Khsiba (1), A. Ben Mohamed (1), M. Mahmoudi (1), G. Gharbi (1), M. Yakoubi (1), M. Medhioub (1), L. Hamzaoui (1) / [1] University hospital of Mohamed Taher Maamouri Nabeul, Nabeul, Tunisia, Gastroenterology.

Introduction: Sustained virological response (SVR) improves the prognosis of patients with hepatitis C virus (HCV)-related cirrhosis. However, hepatic recompensation occurs in only a limited proportion of patients.

Aim: This study aimed to identify predictive factors associated with recompensation after SVR..

Methods: A retrospective study was conducted in the Hepato-Gastroenterology Department of Taher Maamouri Hospital in Nabeul, including 52 patients with decompensated HCV-related cirrhosis followed between 2013 and 2022. Demographic, clinical, laboratory, and prognostic data were collected before and after SVR. Hepatic recompensation was defined according to the Baveno VII consensus (2022) as the fulfilment of all the following criteria: (a) cure or suppression of the primary aetiology (HCV elimination), (b) resolution of ascites (off diuretics), hepatic encephalopathy (off lactulose/rifaximin), and absence of recurrent variceal bleeding for at least 12 months, and (c) stable improvement in liver function (albumin, INR, bilirubin). Statistical analyses were performed using SPSS version 25.

Results: The mean age was 66 ± 8.5 years (range 45–80), with a female predominance (76.9%). The mean follow-up duration was 27 ± 14 months. Genotype 1C was predominant (96.2%), with a mean baseline HCV RNA level of 6.09 ± 0.86 $\log_{10}$ IU/mL (range 3.9–7.9). Before antiviral therapy, ascitic decompensation was present in 80.8% of patients; 94.2% had a Child–Pugh score $\geq$ B7, and the mean MELD score was 15.6 ± 4 . During follow-up, 7 deaths (13.5%) and 4 cases of hepatocellular carcinoma (7.7%) were recorded. Following SVR, hepatic recompensation occurred in 21 patients (40.4%) after a mean of 15.8 ± 15.6 months. In univariate analysis, factors associated with recompensation were: absence of metabolic syndrome ($p < 0.001$), baseline Child–Pugh $\leq$ B9 ($p = 0.001$), lower MELD and MELD-Na scores ($p < 0.001$), lower baseline HCV RNA ($p < 0.001$), and presence of baseline cytopenia ($p = 0.002$). In multivariate analysis, lower baseline HCV RNA was the only independent predictor of hepatic recompensation ($p = 0.001$).

Conclusions: Hepatic recompensation after SVR was achieved in 40.4% of cases. Baseline viral load was the main independent predictive factor of this favourable outcome. These results highlight the importance of early management of cirrhotic patients to optimize their chances of recompensation.

-B01-

FUNCTIONAL REPROGRAMMING OF INTESTINAL MACROPHAGES BY GLIAL SIGNALS. Y. Chen (1), D. Cicia (1), B. Ke (1), S. Santhosh (1), M. Tu (1), M. Dubelloy (1), G. Matteoli (1) / [1] Translational Research Centre for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism.

Introduction: Postoperative ileus (POI) represents a frequent and burdensome iatrogenic complication following abdominal surgery, characterized by a transient inhibition of gastrointestinal motility. While the pathophysiology involves complex neuro-immune interactions, our understanding of the resident immune niche within the intestinal muscularis externa (ME) remains incomplete. Unlike mucosal populations, muscularis macrophages (MMs) reside in intimate anatomical proximity to Enteric Glial Cells (EGCs), suggesting a critical functional coupling. Recent single-cell transcriptomics have highlighted the heterogeneity of MMs. Notably, Lipid-Associated Macrophages (LAMs) have been identified in various diseases as key drivers of efferocytosis and tissue repair. However, whether a specific LAM subpopulation participates in the resolution of acute surgical trauma in the gut remains unknown. We hypothesize that EGCs act as active immune “educators” within the muscularis niche, driving macrophage polarization toward a protective LAM phenotype via specific glial-derived signals.

Aim: This study aims to decipher the molecular and spatial dialogue between EGCs and MMs during POI. Specifically, we sought to determine the functional necessity of LAM-associated genes and receptor signaling for recovery from POI. Furthermore, we aimed to establish an optimized single-nucleus RNA sequencing (snRNA-seq) workflow for the connective tissue-rich muscularis layer to enable high-resolution analysis of ENS-immune interactions. Finally, the study was designed to uncover the cellular mechanisms by which EGCs drive this specific LAM response, focusing on the clearance of apoptotic neural cells.

Methods: POI was induced in mice via a standardized Intestinal Manipulation (IM) model. To ensure tissue specificity, the muscularis externa was meticulously dissected, excluding the mucosa. Our experimental strategies incorporated macrophage-specific conditional knockout (cKO) mice targeting key LAM genes and the administration of Fc-muted blocking antibodies to inhibit specific receptors without Fc-mediated phagocytosis. The immune landscape was comprehensively characterized via high-parameter spectral flow cytometry, while spatial interactions were visualized using high-resolution confocal imaging. Mechanistically, we developed an optimized nuclei isolation protocol for the muscularis tissue to facilitate downstream snRNA-seq analysis.

Results: Phenotypic validation revealed that macrophage-specific cKO and receptor blockade significantly exacerbated POI pathology compared to controls. The intervention groups exhibited delayed resolution of inflammation, sustained pro-inflammatory cytokine levels, and prolonged intestinal transit times. Notably, we observed a marked accumulation of apoptotic cells within the ENS, suggesting a critical defect in the clearance of damaged cells when the LAM pathway is compromised. To investigate the molecular basis of these phenotypes, we established a robust snRNA-seq pipeline for the muscularis. Validation with 10x Genomics kits confirmed high-quality nuclei isolation, overcoming fibrous tissue challenges. This platform successfully captured sufficient numbers of EGCs and enteric neurons, enabling high-resolution analysis of neuro-immune interactions previously inaccessible with conventional methods. High-resolution imaging in EGC reporter mice subsequently revealed that blocking the key receptor signal significantly reduced the number of macrophages phagocytosing damaged EGCs post-IM. This confirms that the “EGC-LAM axis” is essential for efferocytosis, preventing the accumulation of cellular debris that otherwise fuels secondary inflammation and impedes neural recovery.

Conclusions: This study defines the “EGC-LAM axis” as a pivotal protective pathway in POI. Our data demonstrate that EGCs actively initiate a LAM-like macrophage polarization via specific receptor interactions. This process endows macrophages with the efferocytic capacity to clear surgically damaged glial cells. Targeting this clearance mechanism to promote LAM polarization offers a novel therapeutic strategy to accelerate postoperative recovery.

-B02-

MIR-146A REGULATION OF ENTERIC GLIAL CELL REACTIVITY. R. Jehoul (1), J. Vranken (1), A. Holland (1), L. Mombeek (1), M. Gijbels (2), S. Wohl (3), V. Melotte (2) / [1] Hasselt University,

Hasselt, Belgium, Biomedical Research Institute, [2] Maastricht University Medical Centre, Maastricht, The Netherlands, Department of Pathology, [3] The State University of New York, New York, Belgium, Department of Biological and Vision Sciences.

Introduction: Enteric glial cells constitute a peripheral population of neuroglia that are part of the enteric nervous system (ENS). Closely associated with enteric neurons and their projections, enteric glia form an extensive network throughout the gastrointestinal tract, contributing to ENS function and maintaining intestinal homeostasis through interactions with epithelial and immune cells. Enteric glial cells exhibit a high degree of phenotypic plasticity, enabling them, for instance, to sense and respond to intestinal injury or inflammation. Under such conditions, they adopt a reactive phenotype characterised by morphological changes and transient alterations in the expression of canonical glial markers such as Glial Fibrillary Acidic Protein (GFAP) and S100 β . Reactive enteric glia also upregulate pro-inflammatory genes and show elevated expression of immune signalling mediators, underscoring their crucial role in coordinating intestinal immune responses and facilitating tissue repair mechanisms. Recent studies identified that persistent or dysregulated glial reactivity can lead to enteric gliosis, a state in which enteric glia lose their homeostatic functions and instead contribute to neuroinflammation and epithelial barrier dysfunction. Such distorted glial phenotypes are increasingly associated with gastrointestinal motility and inflammatory disorders, highlighting the importance of understanding the molecular mechanisms that regulate enteric glial reactivity. MicroRNAs have been identified as crucial regulators of cellular states during physiological and pathological processes. These endogenous, non-coding RNA molecules, approximately 22 nucleotides in length, control gene expression by modulating the translation and stability of their target mRNAs. Preliminary data indicate that distinct microRNA signatures mark enteric glial identity and suggest the involvement of miR-146a-5p in regulating enteric glial cell reactivity.

Aim: Our goal is to elucidate the miR-146a-5p regulation of enteric glial cell reactivity.

Methods: We combine primary enteric glial cell culture experiments, *in silico* target gene analyses, and *in vivo* mouse assays.

Results: First, using an *in vitro* model of enteric glia reactivity induced by lipopolysaccharide (LPS) and interferon- γ (IFN- γ) treatment, we found a time-dependent elevation of miR-146a-5p transcript levels. Overexpression of miR-146a-5p attenuates LPS+IFN- γ -induced reactivity in enteric glia by downregulating pro-inflammatory gene expression, leading to reduced nitric oxide production and normalization of enteric glia morphology. Conversely, inhibition of miR-146a-5p exacerbates enteric glia reactivity. This was validated *in silico*, where microRNA-mRNA target interaction analyses showed several targets of miR-146a-5p to be involved in immune signalling and inflammatory responses. Moreover, KEGG pathway enrichment analysis of miR-146a-5p targets identified multiple signalling pathways linked to gastrointestinal disorders associated with enteric glial cell reactivity. Conditional inactivation of miR-146a-5p in enteric glial cells using Sox10-CreERT2 mice did not impact ENS organisation or gut function during steady-state conditions. However, in a model of experimental colitis, we identified a significant increase in the number of distorted enteric glia in the absence of miR-146a-5p. In our current experiments, we are investigating how this relates to the level of intestinal inflammation, immune cell activation and overall disease progression.

Conclusions: Together, our findings identify miR-146a-5p as a key regulator of enteric glial cell status, acting to restrain enteric glia reactivity by preserving glial morphology and inhibiting excessive inflammatory responses.

-B03-

PERIPHERAL INFLAMMATION INDUCED BY BACTERIAL AMYLOID CURLI EXACERBATES NEUROINFLAMMATION IN THE APPNL-G-F/MAPT MODEL FOR ALZHEIMER'S DISEASE. A. Hofkens (1), R. Verboven (1), D. De Neve (1), C. Milián Alastruey (2), J. Ott (1), N. De Loose (1), K. Grando (3), C. Tükel (3), J. Timmermans (1), E. Pasciuto (2), W. De Vos (1), P. Verstraelen (1) / [1] University of Antwerp, Antwerp, Belgium, Laboratory of Cell Biology & Histology, [2] University of Antwerp, Antwerp, Belgium, VIB Centre for Molecular Neurology, [3] Temple University, Philadelphia, United States, Centre for Microbiology and Immunology.

Introduction: Dysbiosis and intestinal inflammation are important comorbidities of Alzheimer's disease (AD), but the causality and exact mediators of this gut-brain interplay remain to be characterized. In our previous work, we identified the bacterial amyloid curli, produced by the gut microbiome, as a potent trigger of enteric immune responses, typified by a lasting, systemic production of serum amyloid A3 (SAA3).

Aim: Since serum amyloids (SAAs) can penetrate the blood-brain barrier and are elevated in AD patients,

we now asked to what extent peripheral exposure to curli would influence brain pathology in the APPnl-g-f/MAPT knock-in mouse model of Alzheimer's disease.

Methods: Eight-month-old APPnl-g-f/MAPT mice received an intraperitoneal injection of either curli or PBS. Circulating SAA levels and Saa3 expression in brain were quantified. Additionally, CD45+/CD11b+ myeloid cells were isolated from the brain for bulk RNA sequencing, and key transcriptional changes were validated using RNAscope.

Results: Intraperitoneal curli injection induced both elevated SAA levels in the circulation as well as local Saa3 expression in meninges, choroid plexus, and perivascular cells. Since SAAs promote their cognate gene expression, we hypothesize that these brain regions are directly exposed to the SAAs generated in the periphery. CD45+/CD11b+ myeloid cells, isolated from the mouse brain of curli-injected APPnl-g-f/MAPT mice, displayed a pro-inflammatory transcriptional signature as compared to their PBS-injected counterparts. Validation with RNAscope revealed a significant influx of calprotectin-positive (S100a8/9 expressing) cells and upregulation of microglia activation markers *Fcgr2b*, *Spp1*, and *Msr1* adjacent to amyloid deposits. Currently, we are investigating the causal contribution of SAAs to this response using genetic modulation, and evaluating the impact on AD pathology progression.

Conclusions: Thus, our findings reveal a first mechanistic connection between bacterial amyloids, peripheral immune signalling, and central inflammation.

-B04-

CIRCADIAN PERTURBATION ALTERS GUT TRANSCRIPTOME RHYTHMICITY IN HUMAN INTESTINAL ORGANOID. A. Denis (1), G. Vanotti (1), T. Thijs (1), A. Dubois (2), H. Leng (1), E. Deleus (3), M. Lannoo (3), B. Van Der Schueren (4), L. Ceulemans (2), K. Wagner (5), I. Depoortere (1) / [1] KUL - University of Leuven, Leuven, Belgium, Gut Peptide Research Lab, Translational Research Centre for Gastrointestinal Disorders (TARGID), [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Leuven Intestinal Failure and Transplantation (LIFT) Centre, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Abdominal Surgery, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Endocrinology, [5] University of Vienna, Vienna, Austria, Department of Nutritional Sciences.

Introduction: The circadian system consists of biological clocks that are present throughout the body and align physiological processes with our rhythmic environment through external cues. In the intestine, circadian clocks are regulated by the central clock located in the suprachiasmatic nucleus of the hypothalamus via the light-dark cycle and locally by feeding cues. Chronic disruption of circadian rhythms, as occurs in rotating shift work, obesity and intensive care unit (ICU) stays, increases the risk of developing metabolic and intestinal disorders. Because direct assessment of diurnal rhythms in the human gut over a 24-hour cycle is technically challenging, we employed human 3D intestinal organoids (enteroids) as an alternative model.

Aim: This study investigated the rhythmic expression of clock genes and the gut transcriptome in 3D enteroids derived from the jejunum of patients with obesity and normal-weight organ donors who stayed in the ICU before tissue procurement, two conditions known to disrupt circadian rhythms.

Methods: Jejunal enteroids from normal-weight organ donors (OD, n=8) and patients with obesity (OB, n=8) were synchronized with dexamethasone, and mRNA was collected every 4 hours over 28 hours. The rhythmicity in the expression of core clock genes and the entire gut transcriptome was analysed using bulk RNA-sequencing and confirmed by RT-qPCR. Rhythmicity in intestinal lipid metabolism was investigated using Oil Red O staining.

Results: RNA-seq analysis revealed that 8 out of 16 clock genes were rhythmic in OB while only 2 clock genes were rhythmic in OD enteroids. RT-qPCR analysis confirmed that the mRNA expression of the core clock genes *BMAL1* (peak: ZT 13.25 hours) and *NR1D1* (peak: ZT 18.91 hours) were rhythmic ($P<0.05$) in OB enteroids but not in OD enteroids. In contrast, at the whole-gut transcriptome level, 15% of the transcripts were rhythmic in OD compared to only 2% in OB. Principal component analysis showed that age of patients contributed substantially to inter-individual variability in OB but not in OD enteroids, leading to an underestimation of the number of rhythmic genes in OB enteroids. Including age as a covariate in the statistical model revealed that 10% of transcripts were rhythmic in OD and 7% in OB. Yet, only 0.75% were common to both populations, indicating largely distinct rhythmic genes. Furthermore, gene ontology analysis confirmed that the regulation of circadian rhythms was enriched in OB enteroids but not in OD enteroids. Lipid metabolism remained rhythmic in both populations. Consistently, Oil red O staining confirmed that lipid droplets accumulation was rhythmic in OB ($P=0.09$) and OD ($P<0.05$) enteroids.

Conclusions: The absence of photic (eyes closed, brain death) and behavioural cues (constant fasting, resting and sleeping state) in organ donors before tissue procurement caused a more severe form of chronodisruption than obesity, which is characterized solely by dysregulated behavioral cues. Despite chronodisruption of the core clock machinery, both enteroid populations retain distinct rhythmic transcripts, including shared oscillations in lipid metabolism. Overall, our findings show that disruptions in diurnal rhythmicity are imprinted in 3D enteroids, supporting their use as a platform to identify genes for chronotherapy.

-B05-

INTESTINAL EPITHELIAL CELLS ALTERATIONS IN ALCOHOL USE DISORDER (AUD)
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Introduction: Alcohol Use Disorder (AUD) defined by uncontrolled or excessive alcohol use is associated with more than 200 health diseases resulting in several organs damage. Increasing evidence indicates that gut barrier dysfunction in individuals with AUD plays a critical role in the pathogenesis of alcohol-associated liver disease, a major cause of alcohol related mortality and morbidity. However, the pathophysiological processes that lead to alcohol-induced intestinal epithelium barrier alterations remain poorly understood and need to be addressed.

Aim: Our in vivo data in humans indicate a profoundly disturbed proliferation-differentiation program in AUD patients. In this context, we have established an Intestinal Organoid (Enteroid) model susceptible to partially recapitulate the alterations observed in AUD. Using this model, we aim to investigate morphological changes as well as the impairment of key signaling pathways identified in vivo. Finally, the model will be used to establish a cause-effect relationship between alcohol exposure and the epithelial modifications in AUD.

Methods: Slices of duodenal biopsies derived from healthy and AUD patients were stained by multiplex immunofluorescence to localize the differentiated and undifferentiated epithelial cells. Enteroids were generated from crypts isolated from control and AUD patients' duodenum biopsies by enzymatic digestion, and subsequently grown in 3D (imbedded in Matrigel) and in 2D (on transwell coated with Matrigel). Then, these 3D and 2D models were treated with increasing ethanol concentrations. Gene and protein expression were quantified by qPCR and Immunofluorescence respectively.

Results: AUD patients displayed morphological alterations associated with increased cell proliferation and a modification of the stem cell pool at the crypt base. Ki67+ and CHGA+ cells were increased in AUD patients compared to Healthy subjects. Furthermore, ethanol treatment stimulated proliferation in the 2D enteroids model. In contrast, Wnt canonical pathway is not involved in the proliferation induced by ethanol in the enteroids as observed in vivo.

Conclusions: Proliferation is increased in AUD patients in vivo both in the crypt base and the transit amplify zone. Moreover, duodenal biopsy derived enteroids constitute a valuable model to investigate alcohol-induced epithelial changes ex vivo.

-B06-

UNVEILING THE MUCIN BLUEPRINT: SINGLE-CELL INSIGHTS INTO INTESTINAL EPITHELIAL DYNAMICS ACROSS INFLAMMATORY BOWEL DISEASES. J. Gassman (1), S. Van Laere (2), B. Oosterlinck (1), J. De Man (1), B. De Winter (1), A. Smet (1) / [1] Laboratory of Experimental Medicine and Paediatrics, University of Antwerp, Antwerp, Belgium, Faculty of Medicine and Health Sciences, [2] Centre for Oncological Research (CORE), University of Antwerp, Wilrijk, Belgium, Integrated Personalized & Precision Oncology Network (IPPON).

Introduction: Mucins are major structural and functional components of the intestinal mucus barrier, forming a protective layer that lubricates the epithelial surface and regulates host-microbiome interactions. Aberrant mucin expression and alterations in epithelial cell composition are recurrent features of inflammatory bowel diseases (IBD), including ulcerative colitis (UC) and Crohn's disease (CD). Despite this, the distribution of individual mucin genes across intestinal cell lineages remains incompletely characterised in healthy and (non-)inflamed IBD tissues. Moreover, it is unclear how mucin expression patterns are remodelled during therapeutic intervention. Single-cell RNA sequencing (scRNA-seq) provides the resolution required to map mucin gene expression across

diverse intestinal cell populations and to identify disease- and treatment-associated alterations, thereby advancing the evaluation of mucins as potential molecular markers to support improved disease diagnosis and management. **Aim:** To generate a single-cell mucin expression atlas of the human intestine by analysing scRNA-seq datasets from healthy controls and UC/CD patients to (i) compare cell-type-specific mucin profiles, (ii) define inflammation-associated dysregulation, and (iii) assess treatment-induced changes following anti-TNF α therapy.

Methods: Three publicly available scRNA-seq datasets were re-analysed using a harmonised workflow, applying consistent annotation of intestinal compartments and cell states, informed by the epithelial classification described in GSE282122. The first dataset (GSE214695) comprised colonic biopsies from healthy controls, UC patients, and CD patients. The second dataset (GSE116222) included colonic biopsies from healthy individuals and UC patients, with paired inflamed and non-inflamed samples. The third dataset (GSE282122) provided longitudinal ileal and colonic biopsies from UC and CD patients before and after adalimumab treatment. Expression levels of 21 mucin genes (MUC1-MUC22) were quantified across annotated cell types to identify mucin-expressing populations and investigate expression dynamics across health, inflammation, and treatment response.

Results: Across all datasets, mucin mRNA expression was largely confined to intestinal epithelial cells, with negligible expression in immune or stromal compartments. Healthy intestinal tissue showed a core mucin repertoire dominated by MUC1, MUC2, MUC3A, MUC4, MUC5B, MUC12, and MUC13, with moderate expression of MUC17 and MUC20, and minimal expression of MUC5AC, OVGP1, and EMCN. Goblet cells displayed the highest mucin expression levels, particularly MUC1, MUC2, MUC4, MUC5B, MUC12, and MUC13. BEST4/OTOP2 cells and crypt-top colonocytes were enriched for MUC12 and MUC13. LGR5* stem cell, transit-amplifying, and undifferentiated enterocyte populations exhibited consistent expression of the core mucin repertoire. In contrast, enteroendocrine and tuft cells consistently showed uniformly low expression across both healthy and IBD cohorts. Inflamed UC and CD samples exhibited highly similar mucin dysregulation patterns, indicating shared epithelial responses to inflammation. Goblet cells demonstrated increased expression of MUC1 and MUC12, while crypt-top colonocytes and BEST4/OTOP2 cells showed upregulation of MUC1, MUC3A, and MUC4. LGR5* stem cells exhibited downregulation of MUC2, MUC3A, and MUC13, whereas transit-amplifying cells displayed enhanced expression of MUC1, MUC2, MUC4, and MUC5B. Non-inflamed UC regions showed expression patterns closely resembling healthy controls, supporting inflammation-dependent rather than disease-specific mucin disturbances. Longitudinal analysis following adalimumab therapy revealed region-specific modulation, with increased MUC2 and MUC5AC expression in ileal goblet cells, reduced expression of both genes in colonic goblet cells, a consistent decrease in MUC5B across goblet subsets, and increased MUC12, MUC13, and MUC20 in colonic enterocytes after treatment.

Conclusions: This integrated single-cell analysis provides a comprehensive mucin expression atlas across intestinal epithelial cell types in health, IBD, and anti-TNF α -treated tissue. It identifies a core mucin repertoire, highlights cell-type-specific dysregulation during inflammation, and demonstrates region-dependent mucin modulation following therapy. These findings emphasise the potential of mucins as molecular markers of mucosal barrier healing and as candidate biomarkers for predicting and monitoring treatment response in IBD.

-B07-

DECIPHERING THE HUMAN COLON CELL HETEROGENEITY IN PARKINSON'S DISEASE. M. Vandeput (1), M. Boesch (2), G. Skoufos (2), A. Mikorska (2), N. Stakenborg (1), E. Modave (1), S. Abouelasrar Salama (2), J. Geurts (2), I. Claes (2), C. Vlachos (2), E. Geeraerts (2), S. Mukherjee (2), K. Vandereyken (2), A. Pančíková (3), K. Theunis (3), S. Kint (2), C. Alar (2), A. Sifrim (4), J. Demeulemeester (5), P. Vanden Berghe (6), P. Verstreken (7), C. Proukakis (8), B. Thienpont (4), S. Aerts (5), T. Voet (4), G. Boeckxstaens (6) / [1] KUL - University of Leuven, Leuven, Belgium, Translational research centre for gastrointestinal disorders (TARGID), [2] KUL - University of Leuven, Leuven, Belgium, Department of Human Genetics, [3] VIB-KU Leuven, Leuven, Belgium, Centre for Brain and Disease Research, [4] KUL - University of Leuven, Leuven, Belgium, Department of Human Genetics; KU Leuven Institute for Single Cell Omics; Aligning Science Across Parkinson's (ASAP) Collaborative Research Network, [5] VIB-KU Leuven, Leuven, Belgium, Centre for Brain and Disease Research; KU Leuven Institute for Single Cell Omics; Aligning Science Across Parkinson's (ASAP) Collaborative Research Network, [6] KUL - University of Leuven, Leuven, Belgium, Translational research centre for gastrointestinal disorders (TARGID); KU Leuven Institute for Single Cell Omics; Aligning Science Across Parkinson's (ASAP) Collaborative Research Network, [7] VIB-KU Leuven, Leuven, Belgium, Centre for Brain and Disease Research; KU Leuven Department of Neurosciences; Aligning

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Introduction: Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the loss of dopaminergic neurons in the substantia nigra and Lewy pathology. Classical motor symptoms include bradykinesia, resting tremors and rigidity. However, the clinical presentation is multifaceted and includes many non-motor symptoms. Up to 80% of PD patients have gastrointestinal (GI) complaints such as constipation, that often occur years before the onset of motor symptoms. Nevertheless, the role of the gut in PD pathophysiology remains unclear.

Aim: Our goal is to build a human multi-omic single-nuclei atlas of the PD colon, thereby elucidating PD-associated cell-type specific alterations.

Methods: To this end, we applied 10X Genomics multiome technology to colon samples from 163 individuals (71 PD patients and 92 controls), enabling simultaneous profiling of chromatin accessibility and gene expression at single-nucleus resolution. Using single-nuclei RNA sequencing, we performed differential gene expression and pathway enrichment analyses to identify PD-associated molecular changes at cell-type resolution. To investigate alterations in cell-cell communication, we conducted a CellChat analysis. In addition, we are leveraging 10X Genomics Xenium spatial transcriptomics to explore the spatial organization of identified cell types.

Results: Following stringent quality control, we constructed a comprehensive single-nucleus atlas of the human colon, encompassing approximately 543,000 high-quality nuclei and 20 distinct cell populations. Further subclustering revealed 82 cellular subtypes, including 7 neuronal, 3 glial, and 14 myeloid clusters. Notably, we observed a consistent upregulation of heat shock proteins (HSP) – key molecular chaperones involved in protein folding – across various cell types in PD, including immune subsets, neurons and glia. On the other hand, several cell types showed downregulation of protein translation. The alterations of those two pathways suggest a reaction to the presence of misfolded proteins or protein aggregates, such as Lewy bodies. In addition, we checked how cell-cell interactions were changed in the PD colon, with a focus on the communication between neurons, myeloids and glia. Interestingly, in PD, we observed an increase of ligand-receptor pairs that are involved in axon guidance and neuronal health, such as semaphorins, netrins, and neurotrophins. This implies an increased communication within the neuron-glia-myeloid unit, a potential mechanism to support enteric neurons that get stressed upon PD.

Conclusions: Using our single-nuclei atlas of the PD colon, we were able to pick up cell-type specific alteration in PD patients, including altered HSP expression, translation and cell-cell communication. This resource will provide novel insights into the involvement of the gut in PD pathophysiology and serve as a valuable tool for the research community.

-B08-

COMPLEMENT COMPONENT 3- EXPRESSING FIBROBLASTS IN INTESTINAL INFLAMMATION AND FIBROSIS IN CROHN'S DISEASE. G. Zanella (1), B. Ke (2), M. Tu (2), K. Kwiecien (2), M. Moro (3), A. Salas (3), B. Verstockt (4), S. Vermeire (4), G. Matteoli (2) / [1] KUL - University of Leuven, Leuven, Belgium, Chrometa- TARGID, [2] Translational Research Centre for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Chrometa- TARGID, [3] Hospital Clinic Barcelona- IDIBAPS- CIBER-EHD, Spain, Inflammatory Bowel Disease Unit, [4] University Hospitals Leuven (UZ Leuven), Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Failure of treatment occurs in more than 60% of the Crohn's disease (CD) patients and current immunomodulatory molecules seem to be insufficient to face this challenge. This highlights the need of new therapeutic targets to address the chronic inflammatory process undergoing in the gut. In our lab we have identified a subset of activated fibroblasts harboring a pro-inflammatory and pro-fibrotic phenotype in inflamed and stenotic CD patients. Interestingly, these fibroblasts express high level of Complement Component 3 (C3). The complement system is known to be dysregulated in context of chronic inflammatory conditions, but his role in CD remains unexplored.

Aim: Here we aim at describing the mechanism of C3+ activated fibroblasts and their role in gut inflammation and promoting fibrosis development. In particular we investigate C3 as a potential therapeutic target for CD.

Methods: To characterize fibroblast subsets in intestinal inflammation and fibrosis, full-thickness ileal

biopsies from CD patients (n=10) were profiled using single-cell RNA sequencing (scRNA-seq) on the 10x Genomics platform. Spatial transcriptomic analysis on Xenium Platform (10x Genomics) was performed to characterize C3+ fibroblasts location within the tissue. ELISA assay was used to confirm Complement activation in CD patients. Intestinal fibroblasts were cultured with monocyte-derived cytokines to confirm their C3 production and activation. To investigate the role of C3+ fibroblasts, COL1A2Crex3fl/fl and littermates were subjected to chronic dextran sulfate sodium (DSS)- induced colitis.

Results: Using single-cell RNA sequencing of inflamed transmural ileum from CD patients, we identified a subset of fibroblasts that are activated by proinflammatory monocytes via production of proinflammatory cytokines such as IL-1 β , IL-1 α , OSM, IFN- γ , TGF- β 1, and TNF- α . These activated fibroblasts exhibited exceptionally high level of complement component C3 (C3), thereby recruiting immune cells and exacerbating intestinal inflammation in CD. Spatial transcriptomic analysis confirmed the pro-inflammatory state of these inflammation- associated fibroblasts at the mucosal and submucosal layers, and showed increased expression of C3 in fibroblasts of CD patients compared to healthy control. Moreover, C3AR1+ macrophages were found in close proximity, suggesting a role of fibroblasts in the recruitment and activation of monocytes. ELISA assay of inflamed and stenotic CD biopsies confirmed increased C3 activation as compared to healthy controls. In vitro stimulation of human intestinal CCD18-Co fibroblasts and human primary fibroblasts with the pro-inflammatory cytokines mentioned above confirmed our transcriptomic findings, showing upregulation of C3 and other genes associated with the complement pathway, along with increased secretion of C3 into the supernatants. COL1A2Crex3fl/fl subjected to chronic DSS- induced colitis showed reduced disease severity, impaired immune recruitment and diminished collagen deposition demonstrating the role of C3+ fibroblasts in supporting the inflammation progression as well as fibrosis development.

Conclusions: Our findings suggest that C3 may act as a central mediator in the crosstalk between activated fibroblasts and the immune system, resulting into a vicious cycle driving chronic intestinal inflammation. Here we confirm previous findings described in rheumatoid arthritis and show that C3 drives fibroblast activation and regulates ECM deposition, thereby promoting development of intestinal fibrosis. Overall, our study suggest C3+ fibroblast as a promising therapeutic target to modulate intestinal inflammation and fibrosis in Crohn's Disease.

-B09-

BONE MARROW-IMPRINTED INNATE IMMUNE TOLERANCE FOLLOWING COLITIS: IMPLICATIONS FOR PSC-IBD PATHOGENESIS. R. Matthys (1), L. Heyerick (1), Z. De Vos (1), L. Morren (1), H. Van Vlierberghe (2), A. Geerts (2), S. Raevens (2), S. Lefere (3), X. Verhelst (2), F. Berrevoet (4), L. Devisscher (1) / [1] Ghent University, Ghent, Belgium, Department of Basic & Applied Medical Sciences, Gut-Liver Immunopharmacology Unit, Ghent University, Ghent, Belgium, [2] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology and Hepatology, Ghent University Hospital, Ghent, Belgium, [3] Ghent University, Ghent, Belgium, Liver Research Centre Ghent, Ghent University, Ghent University Hospital, Ghent, Belgium, [4] Ghent University Hospital, Ghent, Belgium, Department of General, Hepatobiliary Surgery and Liver Transplantation, Ghent University Hospital, Ghent, Belgium.

Introduction: Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disease, characterized by co-occurrence of inflammatory bowel disease (IBD) in up to 80% of PSC patients. The main challenge in this disease remains the lack of therapeutic options, in part due to an incomplete understanding of the underlying disease pathophysiology. To date, it is unclear if and how concomitant IBD contributes to PSC, but we and others point towards a protective role of PSC-IBD. Moreover, monocytes and macrophages play a central role in PSC pathogenesis, and it has been shown that innate immune cells, including monocytes, macrophages and their progeny, can acquire a 'memory' following an initial insult which might contribute to disease in the future, a concept that could be at play in the course of PSC-IBD.

Aim: We aim to elucidate how an episode of colitis shapes innate immune responses in the bone marrow (BM) and how these centrally imprinted responses translate to cholestatic liver disease severity in vivo.

Methods: Mice received 2% of dextran sulphate sodium (DSS) dissolved in drinking water during 5 consecutive days to induce acute colitis. Bone marrow (BM) was isolated at defined timepoints post-colitis and cultured ex vivo to generate bone marrow derived macrophages (BMDMs). BMDMs received a secondary challenge and responses were evaluated by RT-qPCR. To investigate the in vivo consequences of these BM responses, common bile duct ligation (CBDL) was performed to induce acute cholestatic liver disease 8 weeks after DSS exposure, with and without bone marrow transplantations (BMTx). BM of mice that underwent acute colitis was used to confirm our results.

Results: Induction of acute colitis in mice resulted in elevated levels of pro-inflammatory cytokines, including Il1b, Il6, Il12, and TNF alpha in BMDMs for at least 6 weeks post colitis. At 8 weeks post-colitis, inflammatory cytokine levels in the BM had returned to baseline values. Ex vivo restimulation of BMDM isolated 8 weeks post-colitis resulted in reduced expression of glycolysis-associated genes, including mTOR, Hif1 α , and Mct1, indicating the development of an innate immune memory state consistent with immune tolerance. In vivo, cholestatic liver injury induced 8 weeks after colitis resulted in a trend toward reduced expression of inflammatory markers in the liver, including Ccr2, TNF alpha, Nlrp3. Similarly, CBDL-mice that received BM from colitis mice, with a resting phase of 8 weeks before CBDL, showed reduced expression of Ccr2, TNF alpha, Nlrp3, and Ccr5 expression in the liver compared to CBDL-mice that were transplanted with healthy BM post-colitis and prior to CBDL. The expression of metabolic regulators mTOR and Hif1 α was significantly lower in the liver of CBDL-mice receiving DSS-exposed BM, further supporting centrally programmed immune tolerance.

Conclusions: A single episode of colitis induces innate immune memory in bone marrow derived macrophages that persists for at least eight weeks. This memory is characterized by a tolerant phenotype, reflected by reduced inflammatory and metabolic gene expression upon restimulation. Bone marrow transplantation experiments indicate that this tolerant state is encoded at the level of hematopoietic progenitors, highlighting a central BM-driven mechanism that may contribute to innate immune dysregulation relevant to PSC-IBD.

-B10-

PATIENTS WITH SHORT BOWEL SYNDROME SHOW A CELLULAR SHIFT IN LEUKOCYTES COMPARED TO CONTROLS - IMPLICATION FOR INTESTINAL ADAPTATION. L. De Meyere (1), B. Ke (1), A. Verbiest (1), P. Huyghe (1), L. Timmermans (2), K. Geboers (2), G. Matteoli (1), L. Wauters (1), T. Vanuytsel (1) / [1] KUL - University of Leuven, Leuven, Belgium, TARGID, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, LIFT.

Introduction: Intestinal adaptation refers to the compensatory process by which the shortened bowel attempts to enhance nutrient absorption in patients with short bowel syndrome (SBS), although the underlying mechanisms remain poorly understood. Given the profound shift in gut microbial composition and the accelerated transit of undigested nutrients in these patients, we hypothesize that these factors may drive changes in the immune landscape, potentially affecting adaptation positively or negatively. Moreover, previous findings from our group indicate elevated plasma lipopolysaccharide binding protein (LBP) levels in patients with SBS who retain a colon in continuity (SBS-CiC) compared to the healthy controls (HC), suggesting increased intestinal permeability and translocation of bacteria or bacterial components.

Aim: We aimed to study the potentially altered immune landscape of patients with SBS-CiC compared to HC.

Methods: Colonic biopsies were collected during standard colonoscopy in patients with SBS-CiC and HC. Lamina propria cells were isolated, stained and acquired on Sony ID 7000 Spectral Analyser. Gating of viable cells was done using the combination of CD45, CD3, CD4, CD8, CD19, CD20, CD56 and CD27. Analyses were conducted using FlowJo and Prism with unpaired t-tests. Results are shown as mean $\pm$ SD or median (min, max) depending on normality of Shapiro-Wilk test.

Results: Patients with stable SBS-CiC (n=6) with underlying disease including ischemia (n=4), inflammatory bowel disease (n=1), and cancer (n=1), with an age of 61.8 $\pm$ 8.8 years, BMI 22.7 $\pm$ 1.9, length of small bowel (59.2 $\pm$ 37.2 cm), percentage of remaining colon (87.5 (50, 100)%), number of PN days per week (2 $\pm$ 2) treated at our centre, UZ Leuven, and HC (n=5), with no previous gastrointestinal (GI) surgery, active GI disease or burdensome symptoms, were included. A uniform manifold approximation and projection (UMAP) visualization of all leukocytes revealed a distinct cellular shift in SBS compared to HC, identifying 13 separate cell clusters through tracking responders expanding (T-REX) analysis. Preliminary findings indicate an increased presence of leukocytes, B cells, and conventional dendritic cells (DCs), alongside a reduction in T cells—particularly TCR $\gamma\delta$ and CD8 $^{+}$ T cells in patients with SBS-CiC. These observations were further validated by individual gating with a statistically significant increase in leukocytes (45.9 $\pm$ 17.8 vs. 22.56 $\pm$ 12.5 % of viable cells, p<0.05) and memory B cells (19.8 $\pm$ 8.1 vs. 9.4 $\pm$ 4.9 % of leukocytes, p<0.05) and a decrease in T cells (23.0 $\pm$ 5.7 vs. 39.3 $\pm$ 7.4 % of leukocytes, p<0.005) and CD8 $^{+}$ T cells (20.4 $\pm$ 9.3 vs. 40.0 $\pm$ 12.0 % of T-cells, p<0.05).

Conclusions: The altered colonic environment in patients with SBS drives a shift in immune cell populations compared to HC. Our data indicate an amplified inflammatory state, potentially recruiting DCs that promote B-cell survival while suppressing CD8 $^{+}$ T cell activity. We hypothesize this pronounced inflammation may negatively impact the natural process of intestinal adaptation in SBS.

CHARACTERIZATION OF BLOOD VESSEL-ASSOCIATED MACROPHAGES ACROSS LAYERS IN HUMAN INTESTINE. N. Pajk (1), N. Stakenborg (1), M. Delfini (1), E. Modave (1), B. Ke (1), S. Van Remoortel (1), A. Wolthuis (2), A. D'Hoore (2), A. Sifrim (3), T. Voet (3), G. Boeckxstaens (1) / [1] Translational Research Centre for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing (CHROMETA), [2] University Hospitals Leuven (UZ Leuven), Leuven, Belgium, Abdominal Surgery, [3] KU Leuven, Leuven, Belgium, Department of Human Genetics.

Introduction: In the murine small intestine, we have previously identified a population of long-lived submucosal C-X3-C motif chemokine receptor 1 (CX3CR1)+ macrophages (Macs) closely associated with blood vessels. These cells are essential for preserving vascular architecture and gut-vascular barrier integrity. In humans, recent single-cell transcriptomic studies have proposed that lymphatic vessel endothelial hyaluronan receptor 1 (LYVE1)* Macs may similarly associate with blood vessels. However, to date, their exact spatial relationship with blood vessels and potential functional differences in the different layers of the human gut remains unknown.

Aim: Our goal is to map blood vessel-associated Macs in healthy human ileum at single-cell resolution across the different intestinal layers and validate their localization using immunofluorescence imaging.

Methods: Healthy ileal tissue from six patients undergoing ileocolonic resection for colorectal cancer was collected and dissected into mucosa, submucosa, and muscularis externa layer. Each layer was enzymatically digested with Liberase to generate single-cell suspensions, and live monocytes and Macs were subsequently isolated by FACS for single-cell RNA sequencing (scRNA-seq). The transcriptomic signature of LYVE1+ Macs across layers was assessed using the Seurat workflow. Innate data base (InnateDB) was used to perform gene ontology term enrichment to identify biological processes of innate immune response. The 50 most differentially expressed genes of LYVE1+ Macs of each layer were used as an input. To validate localization of LYVE1+ Macs, healthy ileum or colon (n=6) was fixed, stained for von Willebrand factor (VWF), LYVE1 and CD163 markers, followed by tissue clearing and imaged with confocal microscope.

Results: LYVE1+ Macs cluster was identified in each layer by the expression of LYVE1, RNASE1, LGMN, F13A1, and MAMDC2. LYVE1+ Macs were most abundantly represented in the muscularis externa containing dense networks of blood and lymphatic vessels. Across all three layers, LYVE1+ Macs were enriched for pathways like platelet degranulation and activation, clotting cascade, and haemostasis, compared to other Mac subsets. This suggests their close spatial and functional relationship with blood vessels throughout the intestinal wall. Comparison of LYVE1+ Macs across intestinal layers showed that mucosal LYVE1+ Macs exhibit a unique transcriptional profile enriched for chemokines, genes associated with antigen processing and presentation, T cell co-stimulation and epithelial interaction, indicating additional roles in immune surveillance and epithelial homeostasis. In contrast, submucosal and muscularis externa LYVE1+ Macs showed a strong upregulation of genes associated with biological processes such as blood vessel endothelial cell fate specification, in line with their perivascular localization. The transcriptional similarity between submucosal and muscularis externa LYVE1+ Macs, with minor differences in chemotaxis and inflammatory genes, further supports a shared functional niche distinct from mucosal LYVE1+ Macs. To validate the localisation of LYVE1+ Macs relative to the blood vessels, we performed immunohistochemical staining on whole-mount preparations of healthy ileum and colon. LYVE1+ Macs were predominantly enriched around submucosal blood vessels, where they exhibited an elongated morphology with extended processes, that appeared to line and wrap along blood vessels. Importantly, these cells also co-expressed CD163, previously identified as a blood vessel-associated marker in mice. Interestingly, LYVE1+ Macs that were located slightly more distant from blood vessels adopted a more rounded, compact morphology, potentially reflecting their role in vascular protection and tissue surveillance.

Conclusions: Here we identify blood vessel-associated LYVE1+ Mac subset in each layer of healthy ileum using scRNA-seq. Additionally, we show submucosal LYVE1+ Macs to be in intimate contact with blood vessels. Importantly, as in mice, these human blood vessel-associated Macs could also act as guardians of the gut-vascular barrier, and play an important role in gastrointestinal diseases such as inflammatory bowel disease, where gut-vascular barrier is disrupted.

VOLATILE ORGANIC COMPOUND PROFILING IN IRRITABLE BOWEL SYNDROME: A BREATH AWAY FROM AN IBS BIOMARKER? E. Moonen (1), S. Velichkova (1), L. Truyen (1), J. De Man (1), K. Lamote (1), B. De Winter (1), H. De Schepper (2) / [1] Laboratory of Experimental Medicine and

Introduction: Irritable bowel syndrome (IBS) is a disorder of gut-brain interaction for which objective, organic biomarkers are still lacking to facilitate diagnosis, patient stratification and clinical decision-making. IBS diagnosis continues to rely on the symptom-based Rome IV criteria, which do not capture the biological heterogeneity of the disorder. As a result, patient and physician often navigate through a cumbersome trial-and-error treatment process, frequently leading to inappropriate or delayed therapy and limited guidance for personalized treatment. This highlights the critical need for biomarker-driven approaches that potentially reflect underlying disease mechanisms. Volatile organic compounds (VOCs), originating from host metabolism, immune activity, and gut microbiota, have emerged as promising, non-invasive biomarkers that may reflect IBS pathophysiology. Previously, our group demonstrated that breath VOC profiling can accurately discriminate IBS patients from healthy controls, using ion mobility spectrometry, although compound resolution remained insufficient for confident VOC identification.

Aim: Building on previous work, we now apply high-resolution gas chromatography-quadrupole time of flight mass spectrometry (GC-QTOF-MS) to assess whether VOCs differentiate IBS, and elucidate which VOC signatures define and potentially explain IBS pathophysiology.

Methods: This prospective breathomics study included 49 participants: 20 healthy controls (HC) and 29 IBS patients (irrespective of their IBS subtype) fulfilling the Rome IV criteria. Exhaled breath of all participants was collected in Tedlar® bags, and immediately transferred onto Tenax® sorbent tubes. After collection, breath samples were analysed using GC-QTOF-MS. To identify discriminatory VOCs, a machine learning-based feature selection approach was applied, using least absolute shrinkage and selection operator (LASSO) regression. Selected discriminatory VOCs were subsequently examined using univariate statistics and chemical classes were assessed to identify specific compound classes that are enriched in the set of data. Finally, a multivariate model was established to assess their differentiating performance, and they were putatively mapped to pathways.

Results: The median (IQR) age was 28 (15.5) years for IBS patients and 24 (2.5) years for HC, with a comparable sex distribution (76% vs. 80% females, respectively). Median (IQR) BMI was 23.7 (4.6) in the IBS group and 20.8 (2.60) in the HC group. Within the IBS group, 16 patients had diarrhea-predominant IBS, 7 had constipation-predominant IBS, and 6 had mixed-type IBS. From the >1000 detected VOCs, a preprocessing workflow was applied to exclude sporadic VOCs, followed by transformation and standardization for LASSO feature selection. The machine learning model identified three discriminatory VOCs (here referred to as VOC1, VOC2, and VOC3). Subsequent univariate testing confirmed that all three VOCs were significantly enriched in IBS ($p < 0.01$ (Mann-Whitney U)). IBS patients showed higher concentrations of all three VOCs, with VOC1, VOC2, and VOC3 exhibiting log2 fold changes of 3.36, 3.92, and 3.10, respectively (corresponding to ~10-, ~15-, and ~8.6-fold increases). When combining the three VOCs into a multivariate model, the resulting ROC curve showed strong discriminative performance (AUC = 0.84, sensitivity = 0.69, specificity = 0.95, accuracy = 0.80, NPV = 0.68, PPV = 0.95). VOC1 and VOC2 are both considered as potential markers of oxidative stress, inflammation, and microbiome-related alterations. The detection of VOC3 reinforces this, as it is an exclusive oxidation product of isoprene and a well-established proxy for oxidative stress. This VOC signature consistently reflects heightened oxidative stress and altered lipid metabolism.

Conclusions: Volatomic breath profiling in IBS shows great potential for discriminating IBS from HCs, and for defining clinically relevant biomarkers composed of specific VOCs. Nonetheless, the limited sample size might risk model overfitting and introduces uncertainty in the estimates. Further research including larger cohorts is necessary, along with the targeted validation of the identified VOCs to further confirm their mechanistic role in IBS and potentially differentiate the distinct IBS subtypes. Collectively, these findings indicate that the selected VOCs represent highly promising candidate biomarkers for IBS.

-B13-

COMPREHENSIVE EVALUATION OF SMALL-BOWEL INVOLVEMENT IN SYSTEMIC SCLEROSIS: HIGH-RESOLUTION JEJUNAL MANOMETRY PATTERNS AND THEIR CORRELATION WITH ENS AUTOIMMUNITY. L. Alcalá González (1), S. Kulkarni (2), A. Guillen del Castillo (3), F. Felix Tellez (1), M.T Sanz Martinez (4), L. Triginer (3), J. Serra (1), C. Barber (1), C. Codina (3), C. Simeon Aznar (3), L. Viñas (4), J. Perurena (4), C. Malagelada (1), Z. McMahan (5) / [1] Fundació Hospital Universitari Vall d'Hebron - Institut de Recerca, Barcelona, Spain, Digestive System Research Unit, Department of digestive diseases, [2] Harvard Medical School, Boston, United States, Division of Medical Sciences,

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Introduction: Small-bowel involvement is a common and frequently underrecognized complication of systemic sclerosis. Small bowel dysfunction manifests with symptoms of enteric dysmotility such as abdominal pain, distension, nausea, or vomiting, along with objective signs such as malnutrition, small intestinal bacterial overgrowth, and, in severe cases, chronic intestinal pseudo-obstruction. To date, the mechanisms underlying systemic sclerosis-related enteric dysmotility remain poorly defined. **Aim:** To evaluate whether combining high-resolution jejunal manometry with immunopathological analysis of enteric nervous system (ENS) targets could elucidate mechanisms of small-bowel involvement in systemic sclerosis.

Methods: We conducted a prospective study of consecutive systemic sclerosis patients with moderate–severe gastrointestinal symptoms (January 2018–July 2025). Small-bowel motor function was assessed using a 35-channel high-resolution jejunal manometry catheter, placed under fluoroscopic guidance, during 3h fasting and 2h nutrient infusion. Tracings were analysed qualitatively using established enteric dysmotility criteria and quantitatively using high-resolution parameters (propagation velocity, and contractile vigour), compared with normative values from healthy controls. To explore immunological mechanisms associated with small bowel involvement, serum samples from included patients were incubated with freshly isolated longitudinal muscle–myenteric plexus (LM-MP) preparations from Wnt1-cre:tdTomato neural crest-fate-mapping mice. Immunostaining patterns were assessed and correlated with small bowel motility results.

Results: Forty patients were included (mean age 52 ± 10 years; 95% women; diffuse cutaneous systemic sclerosis = 11, limited cutaneous systemic sclerosis = 29). Overall, 26/40 patients (65%) fulfilled one or more established criteria for enteric dysmotility. The most frequent abnormalities were irregular or uncoordinated non-propagated activity (12/40, 30%), bursts >2 min (8/40, 20%), and simultaneous spastic contractions (4/40, 10%). Phase III complex evaluation revealed abnormal configuration with simultaneous and/or retrograde propagation in 5/40 patients (17%), and absent fasting phase III complexes in 13/40 (33%). During nutrient infusion, minute rhythm pattern >30 min in the absence of mechanical obstruction occurred in 8/40 (20%), and discrete clustered contractions in 6/40 (16%). Quantitative analysis of new high-resolution parameters revealed significant motor impairment in systemic sclerosis compared with healthy controls. Patients showed fewer propagated contractions (median 2 [0-7] vs 7 [4-17] per subject, $p=0.014$), with markedly reduced contractile vigor (96 [292-1142] vs 583 [355-905] mmHg·cm·s, $p=0.012$) during phase II, and slower propagation (6.0 [4.7 - 7.2] vs 11.4 [7.2 - 16.2] cm/min; $p=0.023$) and contractile vigor (3112 (341-6942) vs 6056 (3054-9453) mmHg·cm·s $p=0.002$) of phase III complexes. Postprandial contractile vigor in patients with systemic sclerosis showed wide heterogeneity (median 4100 [341–8181] vs 3492 [1337 – 5091] mmHg·cm·s, $p=0.113$), comparable overall to healthy controls. However, patients with a minute-rhythm pattern ($n=8$) exhibited markedly increased postprandial vigor (8315 [6518–17 456] vs 3492 [1337 – 5091] mmHg·cm·s; $p<0.001$), whereas those with apparently normal postprandial response (without minute-rhythm pattern, $n=32$) showed significantly reduced values (1612 [254–4996] vs 3492 [1337 – 5091] mmHg·cm·s; $p=0.013$). Notably, 9 of the 14 patients (64%) with apparently normal motility by qualitative analysis had abnormal findings on quantitative analysis, including reduced propagated contractions during fasting ($n=4$), low-amplitude phase III complexes ($n=2$), or a decreased postprandial response ($n=3$). In the experimental model, all patients exhibited serum reactivity. Patients with overt enteric dysmotility by established criteria ($n=26$) showed a higher prevalence of diffuse myenteric layer staining (73% vs 27% $p=0.257$). Interestingly, patients with uncoordinated contractile activity but preserved vigor demonstrated increased prevalence of nuclear antigen staining in myenteric plexus cells (78% vs 21%, $p=0.017$) compared to patients with normal coordination but reduced contractile vigor. No relevant differences were observed in mucosal or submucosal staining.

Conclusions: In symptomatic patients with systemic sclerosis, high-resolution jejunal manometry identifies a high prevalence of small-bowel motor abnormalities, including subclinical dysfunction detectable only by high-resolution quantitative analysis. The consistent presence of serum reactivity against myenteric plexus antigens and its association with dysmotility severity support a mechanistic role for ENS-targeting autoimmunity in systemic sclerosis-related small-bowel involvement. These findings suggest that combined physiological and immunopathological evaluation may improve phenotyping and pathobiological understanding of small bowel involvement in systemic sclerosis.

UNCHANGED INTESTINAL BARRIER BUT ENHANCED GLUCOSE UPTAKE IN SHORT BOWEL SYNDROME, INDEPENDENT OF THE ANATOMY TYPE. L. De Meyere (1), A. Viaene (1), J. T Tóth (1), F. Dujardin (1), S. Vrancken (1), L. Timmermans (2), K. Geboers (2), A. Verbiest (1), L. Wauters (1), R. Farré (1), T. Vanuytsel (1) / [1] KUL - University of Leuven, Leuven, Belgium, TARGID, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, LIFT.

Introduction: Intestinal adaptation is the compensatory mechanism of the shortened intestine in patients with short bowel syndrome (SBS), aiming to improve nutrient and fluid absorption. However, this process remains poorly understood and it is unclear how this differs between patients with different anatomy types, e.g. patients with an end-jejunostomy (type I) and patients with a colon-in-continuity (CiC) (type II and III). We hypothesize that adaptation involves not only beneficial changes but also detrimental alterations to the gut physiology, e.g. an impaired barrier function contributing to secretion of fluids and electrolytes and, consequently, greater fluid and electrolyte losses.

Aim: To investigate alterations in intestinal barrier function in patients with SBS compared to controls.

Methods: Patients with stable SBS (n=20, of which 13 with CiC) and controls (n=20) were included in case of no previous GI surgery, active GI disease or burdensome gastrointestinal symptoms. Duodenal and/or colonic biopsies, collected during gastroduodenoscopy and colonoscopy, were mounted in Ussing chambers. Transepithelial electrical resistance (TEER) was measured and the paracellular passage was assessed using a 4 kDa fluorescein isothiocyanate-labelled dextran (FITC-dx4). To assess ion secretion, the amplitude difference in short-circuit current (Isc), needed to keep the potential difference (PD) clamped at 0 mV, was measured after luminal glucose (15mM, to stimulate the Na⁺/glucose cotransporter 1 (SGLT1)) was added. Data are shown as median (min, max).

Results: Duodenal permeability, measured by TEER and FITC-dx4 flux, was similar between patients with SBS with end-jejunostomy, those with a CiC and controls. Furthermore, colonic permeability was similar between patients with SBS-CiC and controls. However, the glucose-induced Isc increase was more pronounced in SBS compared to controls (30.02 (15.83, 76.50) $\mu\text{A}/\text{cm}^2$ ($p<0.005$), but no difference was seen between patients with an end-jejunostomy (55.33 (21.6, 86.9)) $\mu\text{A}/\text{cm}^2$ or CiC (56.33 (30.57, 99.67)) $\mu\text{A}/\text{cm}^2$ ($p=0.64$).

Conclusions: Our findings indicate that patients with SBS do not have an altered intestinal permeability in either the duodenum or sigmoid colon, and duodenal permeability does not differ across the different anatomy types. The observed increase in glucose-induced Isc indicates an enhanced activity of the SGLT1 transporter, facilitating greater glucose absorption and thereby supporting natural intestinal adaptation following resection. Notably, no differences in SGLT1 activation were detected between patients with end-jejunostomy and those with CiC, contrary to our initial hypothesis of different adaptive responses. Further research is ongoing to confirm possible changes of the receptor at DNA or protein level.

IMPAIRED GASTRIC SLOW WAVES AND MITOCHONDRIAL FUNCTIONS IN DIABETIC RATS. O. Athavale (1), C. Driscoll (2), T. Pham (2), K. Smith-Edwards (3), L. Cheng (2), P. Du (2) / [1] University of Auckland, Auckland, New Zealand, Auckland Bioengineering Institute (currently Laboratory for Enteric Neuroscience - KU Leuven), [2] University of Auckland, Auckland, New Zealand, Auckland Bioengineering Institute, [3] Mayo Clinic, Rochester, United States, Department of Physiology and Biomedical Engineering.

Introduction: Diabetes impairs neuromuscular functions of the stomach and has significant clinical implications. The disruption of well-coordinated gastric electrophysiology has been implicated in the disruption of gastric motility function. The aim of this study was to identify the effects of diabetes on gastric slow waves and mitochondrial functions in a rat model of diabetes.

Aim: The aim of this study was to identify the effects of diabetes on gastric slow waves and mitochondrial functions in a rat model of diabetes.

Methods: The study was approved by the University of Auckland Animal Ethics Committee. Male Wistar rats were randomly assigned to the diabetic (n = 6) or control (n = 6) groups. The diabetic group received a high-fat diet over a 12-week period and a low-dose intraperitoneal injection of streptozotocin (25 mg/kg) at week 8 post-diet. At the end-point (week 12), we conducted in vivo slow-wave mapping of the stomach under isoflurane anaesthesia using flexible extracellular electrodes (8 x 4 electrodes, 1 mm spacing) placed on the

gastric serosa. Gastric tissue was excised after completion of the in vivo measurements and respirometry measurements of gastric tissue homogenates were conducted. Blood glucose, slow wave frequency and pattern, and mitochondrial oxygen flux were measured and compared between the two groups.

Results: Blood glucose levels in the diabetic group were higher compared to the control group (16.98 ± 9.36 vs 6.22 ± 0.48 mmol/L, $p < 0.037$). While coordinated, antegrade slow waves did occur in both the control and diabetic groups, the percentage of normal antegrade propagation was reduced in the diabetic group compared to the control group ($91.9\% \pm 0.1\%$ vs $51.6\% \pm 0.4\%$; $p < 0.04$), without a difference in the frequency (3.45 ± 0.70 vs 3.78 ± 0.58 cpm, $p > 0.39$). Diabetic gastric mitochondria showed decreased oxygen flux at the oxidative phosphorylation through complex I and complex II electron inputs (18.19 ± 2.61 vs 4.91 ± 1.87 pmol/s/mg, $p < 0.05$).

Conclusions: We confirmed that diabetes impaired gastric slow wave propagation in anaesthetised rats. The respiration rate of gastric smooth muscle was reduced in diabetic rats.

-B16-

TRAINING-INDUCED IMPROVEMENTS IN INSULINECONOMY IN STANDARD BRED HORSES ARE DISSOCIATED FROM GLUT4/GLUT12 ABUNDANCE IN LOCOMOTOR MUSCLE: INTEGRATING ORAL GLUCOSE TOLERANCE TEST AND FREQUENTLY SAMPLED INTRAVENOUS GLUCOSE TOLERANCE TEST OUTCOMES. L. De Maré (1), B. Boshuizen (2), M. Willems (1), F. Schaafstra (3), J. Melis (3), C. de Meeûs d'Argenteuil (1), K. Goethals (4), J. De Oliveira (5), G. Hosotani (5), D. Deforce (6), F. Van Nieuwerburgh (6), Y. Gansemans (6), L. Devisscher (7), L. Verdegaaal (8), J. Meyer (8), C. Delesalle (1) / [1] Ghent University, Ghent, Belgium, Department of Translational Physiology, Infectiology and Public Health, Research Group of Comparative Physiology, Faculty of Veterinary Medicine, [2] Wolvega Equine Hospital, Oldeholtspade, The Netherlands, Faculty of Veterinary Medicine, [3] HAS Green Academy, DE 's-Hertogenbosch, The Netherlands, University of Applied Sciences for Agriculture, Food and the Living Environment, [4] Ghent University, Ghent, Belgium, Biometrics Research Centre, [5] Cargill, Vilvoorde, Belgium, Research and Development Centre Europe, [6] Ghent University, Ghent, Belgium, Laboratory of Pharmaceutical Biotechnology, Faculty of Pharmaceutical Sciences, [7] Ghent University, Ghent, Belgium, Gut-Liver Immunopharmacology Unit, Department of Basic and Applied Medical Sciences, Faculty of Medicine and Health Sciences, [8] University of Adelaide, Adelaide, Australia, Equine Health and Performance Centre, School of Animal of Veterinary sciences, Roseworthy Campus.

Introduction: In most mammalian athletes, improved insulin sensitivity after training coincides with increased expression of the insulin-responsive glucose transporters GLUT4 and GLUT12 in skeletal muscle. However, recent equine work challenges this paradigm, suggesting that trained horses may reduce total GLUT4/GLUT12 abundance despite better whole-body insulin handling. Given the horse's reliance on mixed fuel strategies, slower glycogen repletion, and substantial contributions of amino-acid and microbiome-derived metabolites to aerobic metabolism, the mechanisms linking training, insulin sensitivity, and muscle GLUT expression require species-specific investigation.

Aim: To determine whether 8 weeks of standardized harness training alters insulin sensitivity (in-feed OGTT; FSIGTT) in Standardbred mares, and whether training-induced changes in insulin sensitivity are associated with changes in total skeletal-muscle GLUT4 and GLUT12 protein abundance at rest and after acute exercise.

Methods: Fifteen untrained Standardbred mares (3–5 years) underwent an 8-week harness-training protocol (4 sessions/week). Before and after training, each horse completed a 10-day metabolic testing sequence consisting of an in-feed oral glucose tolerance test (OGTT) and a frequently sampled IV glucose tolerance test (FSIGTT). OGTT outcomes included Maximum glucose, Time-to-Peak glucose, AUC glucose, Maximum insulin, AUC insulin, Time-to-Peak insulin, and AUC glu/AUC ins. FSIGTT outcomes included insulin sensitivity (SI), glucose effectiveness (Sg), acute insulin response to glucose (AIRg), and disposition index (DI), determined by MINMOD. Muscle biopsies (vastus lateralis) were collected in 11 horses at rest and 10 minutes post-acute exercise, both pre- and post-training. Total protein expression of GLUT4 and GLUT12 was quantified by Western blot and normalized to GAPDH. Training effects were evaluated using paired tests or non-parametric equivalents; correlations between transporter abundance and insulin indices used Spearman's ρ ($\alpha = 0.05$).

Results: Training significantly altered insulin economy during OGTT. Maximum insulin decreased ($P = 0.005$), AUC insulin decreased ($P = 0.0015$), and Time-to-Peak insulin increased ($P = 0.034$), indicating improved systemic insulin handling and a lower insulin requirement to dispose of an identical oral glucose load. Conversely, OGTT glucose variables showed no significant overall changes. FSIGTT indices (SI,

Sg, AIRg, DI) did not change significantly, although a non-significant tendency toward a lower AIRg was observed. Training and acute exercise markedly affected muscle GLUT expression. Total GLUT4 did not differ at rest, but decreased significantly after acute exercise in the trained compared to the untrained state ($P = 0.02$). GLUT12 decreased overall after training ($P = 0.04$) and showed a stronger decline in acute post-exercise samples ($P = 0.003$). Thus, training did not upregulate either transporter and instead reduced total GLUT4/GLUT12 in locomotor muscle. Correlational analyses demonstrated selective associations. Acute GLUT12 expression in the untrained state correlated positively with Maximum_insulin ($\rho = 0.66$; $P = 0.028$) and AUCinsulin ($\rho = 0.66$; $P = 0.026$). After training, the reduction in acute GLUT12 correlated negatively with Time-to-Peakinsulin ($\rho = -0.61$; $P = 0.048$). No significant associations were detected between GLUT4/GLUT12 and FSIGTT parameters.

Conclusions: Eight weeks of standardized harness training improved insulin economy during OGTT but did not enhance insulin sensitivity indices derived from IV glucose challenge. Importantly, these functional improvements occurred despite—and in parallel with—decreases in total GLUT4 and GLUT12 protein abundance in vastus lateralis muscle, especially after acute exercise. This dissociation from the canonical human/rodent paradigm suggests that training improves whole-body insulin effectiveness in horses through mechanisms other than up-regulation of muscle GLUT4/GLUT12, potentially via splanchnic handling, incretin effects, hepatic extraction, and expanded availability of alternative insulin-dependent fuels (branched-chain/aromatic amino acids, acetate, microbiome-derived substrates). The OGTT appears more sensitive than FSIGTT for detecting training-related adaptations in horses. Overall, these findings support a species-specific metabolic model in which trained equine muscle shifts away from a glucose-centric phenotype toward diversified substrate use, rendering GLUT4/GLUT12 total abundance a poor predictor of improved insulin economy in equine athletes.

CASE REPORTS

-C01-

A RARE CAUSE OF DYSPHAGIA: OEOSOPHAGAL STENOSIS DUE TO IGG4 DISEASE FROM DIAGNOSIS TO MANAGEMENT. L. Triki (1), L. Verset (2), M. Ilzkovitz (3), A. Beun (4), P. Eisendrath (1) / [1] ULB Saint-Pierre, Brussels, Belgium, Gastroenterology, [2] HUB Hôpital Erasme, Brussels, Belgium, Department of Pathology of HUB Erasme Hospital Brussels, [3] Hôpitaux Universitaires de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Belgium, Department of Internal Medicine of HUB Erasme Hospital, [4] ULB Saint-Pierre, Brussels, Belgium, Department of Internal Medicine of CHU Saint-Pierre Hospital.

IgG4-related disease (IgG4-RD) is a recognized systemic fibro-inflammatory condition characterized by a dense lymphoplasmacytic infiltrate rich in IgG4-positive cells and storiform fibrosis. Although initially described in pancreatic affections in 2001 and 2003, it is now known to affect virtually every organ, including the biliary tract, salivary glands, pancreas, kidneys, lungs for example, and rarely, the oesophagus. Diagnosis relies on a constellation of criteria: elevated serum IgG4 levels, characteristic histopathology (lymphocytic infiltration, obliterative phlebitis, and storiform fibrosis with organ-specific diagnostic criteria), and location.

We report the case of a 47-year-old female patient with a medical history including three episodes of acute pancreatitis, two episodes of pyelonephritis, and insulin-requiring type 2 diabetes. She presented for evaluation of dysphagia that had been evolving over two years. Endoscopy revealed a benign appearing stricture impassable by an adult endoscope. An upper gastrointestinal series and an abdominal CT scan confirmed the presence of marked oesophageal wall thickening and a regular stricture in the middle third of the oesophagus. A subsequent PET-CT scan showed an isolated hypermetabolism of the oesophageal walls, suggestive of an oncological or an inflammatory process. Endoscopic ultrasound (EUS) was performed due to parietal mucosal thickening, followed by submucosal wall tissues acquisition with fine needle biopsy (FNB). Histological results from the FNB demonstrated a lymphoplasmacytic infiltrate with an IgG4 quantification of 22 cells per 40x high-power field (HPF), highly suggestive for the diagnosis of IgG4-RD. Screening for other organ involvement revealed suspected renal and myocardial affection. Treatment with corticosteroids (dose?) was significantly delayed due to the presence of latent tuberculosis infection and poorly controlled diabetes, which was further dysregulated by the use of corticosteroids. A concomitant corticosteroid-sparing regimen with azathioprine was attempted in view the adverse effects associated with corticosteroid treatment but did not lead to clinical improvement. Ultimately, treatment with Rituximab was initiated after 9 months, resulting in the beginning of symptomatic improvement. This case highlights, a rare cause of dysphagia (oesophageal IgG4-RD) and, the significant difficulty in managing this condition due to the patient's complex comorbidities (diabetes, latent tuberculosis). The certainty of the diagnosis and the follow-up of the treatment in this case necessitate a multidisciplinary approach and close cooperation.

-C02-

CROHN'S OFF TRACK: AN UNEXPECTED JOURNEY INTO THE LUNGS. G. Debbarh (1), A. Cremer (1), L. Amininejad (1) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Gastroenterology.

A 36-year-old woman living in Belgium presented with febrile pancytopenia at the emergency department. Her medical history included Crohn's disease A2B2L3 with ano-perineal involvement and extra-intestinal features such as arthropathy, psoriasis and primary sclerosing cholangitis. Previous treatments included azathioprine and infliximab, which had been discontinued more than 3 months earlier due to suspected anti-TNF-induced lupus. She had recently completed a three-dose course of methotrexate and was on no other active treatment. Laboratory tests revealed neutropenia ($700/\text{mm}^3$), thrombocytopenia ($143,000/\text{mm}^3$), mild anaemia ($3,080,000/\text{mm}^3$) and slightly elevated C-reactive protein (16 mg/L). Thoraco-abdominal CT showed an active ileocolonic inflammation as well as bilateral nodular pulmonary opacities suggestive of granulomatous pneumonitis. Extensive infectious workup was performed. Bronchoalveolar lavage (BAL) cultures for aerobic bacteria, fungi and mycobacteria were negative, as was auramine staining. Viral PCRs for influenza A/B, parainfluenza, adenovirus, RSV and metapneumovirus were all negative. CMV and Pneumocystis Jireovicii PCRs, Aspergillus antigen, Quantiferon assay and gastric aspirate cultures for mycobacteria were also negative. Empirical broad-spectrum antibiotics were started, leading to clinical and biological improvement within 10 days. Despite this improvement, follow-up imaging three weeks later showed persistent pulmonary nodules. Repeat microbiological assessments again yielded negative results.

A second BAL showed increased lymphocytes (22%) and neutrophils (44%) with normal eosinophils and a normal CD4/CD8 ratio. Transbronchial biopsies showed macrophage-rich inflammatory infiltrates without neoplastic cells. Serum ACE levels were normal, providing no evidence for sarcoidosis. Given the persistence of radiologic abnormalities, the absence of infection or neoplasia, and the long-standing withdrawal of anti-TNF before the onset of pulmonary lesions, a systemic IBD-related pulmonary manifestation was suspected. Infliximab monotherapy was reintroduced along with ursodeoxycholic acid. The patient experienced rapid improvement in digestive symptoms and complete radiologic resolution of pulmonary lesions. This evolution strongly suggested that the pulmonary findings were a rare extra-intestinal inflammatory manifestation associated with Crohn's disease rather than infection, drug toxicity or malignancy. This case underlines the complexity of assessing pulmonary lesions in immunomodulated patients with chronic inflammatory disease. Thorough exclusion of infectious and neoplastic aetiologies is essential, as appropriate IBD-directed therapy may lead to complete clinical and radiologic resolution.

-C03-

HOW CAN YOU MEND A BROKEN HEART? A RARE CASE OF A PERICARDO-GASTRIC FISTULA. V. VandenDriessche (1), E. Kaya (1), S. Djellout (2), G. Verset (3), A. Lemmers (1), F. Tannouri (2) / [1] Hôpitaux Universitaires de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Belgium, Gastroenterology, [2] Hôpitaux Universitaires de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Belgium, Interventional radiology, [3] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology.

We report the case of a 74-year-old man presenting with progressively worsening chest pain over the course of one month. His medical history was notable for locally advanced, multifocal hepatocellular carcinoma (HCC). Initial treatment consisted of transarterial radioembolisation (TARE) of hepatic lesions located in segments VII/VIII and II/III, along with bland embolisation of segment IVb. Systemic therapy with atezolizumab combined with bevacizumab was subsequently introduced, followed by transarterial chemoembolisation (TACE) targeting a lesion in segment II. Stereotactic body radiotherapy (SBRT) was later performed for a progressing component in the same segment. Upon subsequent evidence of oligo-progression, systemic therapy was switched to sorafenib. During follow-up, the patient developed progressive retrosternal chest pain 16 months post-SBRT, prompting cardiac evaluation. Initial investigations excluded myocarditis or an ischaemic origin. However, transthoracic echocardiography revealed pericardial fluid and the presence of air within the pericardial cavity. These findings were confirmed by computed tomography (CT), which additionally demonstrated a fistulous tract communicating between the stomach and the pericardium, associated with pneumopericardium. Pericardio-gastric fistulae are exceptionally rare clinical entities, with fewer than one hundred cases reported in the literature. Their aetiology is most often related to malignant invasion, postoperative complications, or iatrogenic injury following local therapies such as radiotherapy or radiofrequency ablation. Given their rarity, no established management guidelines exist. Treatment strategies range from conservative management to surgical repair, depending on the patient's condition and the underlying cause. Although thoracotomy has been associated with reduced mortality, it was considered too high-risk in our patient. Concerns regarding impaired wound healing and the potential for further fistulisation under sorafenib therapy, compounded by prior radiotherapy exposure, rendered both surgical and endoscopic interventions unsafe. A minimally invasive approach was performed by the interventional radiology team using Cone Beam CT (CBCT), fluoroscopy and ultrasound guidance. Under local anaesthesia, a percutaneous puncture of the stomach was performed and a 4 Fr sheath was inserted in order to opacify the stomach and therefore the fistula tract with air. The fistula tract was then seen on the lateral projection and a puncture under fluoroscopy was performed. The puncture was complicated by bleeding from the internal thoracic artery, which was promptly managed with per-procedural Glue embolisation. Then a CBCT was performed confirming the good positioning of the needle. A hydrophilic wire was advanced into the stomach and a 4 Fr sheath was inserted. An 8 mm vascular plug was positioned within the tract, followed by embolisation using a 1:1 diluted glue mixture to achieve complete occlusion. The patient experienced a rapid clinical improvement, with complete resolution of chest pain and no recurrence of pneumopericardium. Oral intake was progressively reintroduced, and prophylactic antibiotic therapy was discontinued. No clinically significant post-procedural complications were observed during the one month follow-up. Endoscopic follow-up 30 days after the procedure revealed confluent mucosal scar tissue along the lesser gastric curvature and confirmed the absence of a residual pericardio-gastric fistula. This case illustrates a rare occurrence of a pericardio-gastric fistula secondary to advanced hepatocellular carcinoma and prior locoregional and systemic therapies. The successful percutaneous management supports the role of image-

guided interventional techniques as a safe and effective alternative to surgery especially in high-risk patients for whom conventional treatment options are not feasible.

-C04-

CASE REPORT : FROM BOWEL TO LUNG : THE UNEXPECTED PULMONARY CAUSE OF A RELENTLESS DIARRHEA. A. Lannoy (1), A. Deceuninck (2), J. Dargent (3), V. Lamberts (4), C. Bouvy (5), D. Glorieux (6), Z. Issa (7) / [1] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, Internal Medicine, [2] GHDC, Charleroi, Belgium, Radiology, [3] Institut de Pathologie et de Génétique, Charleroi, Belgium, Pathology, [4] GHDC, Charleroi, Belgium, Pneumology, [5] GHDC, Charleroi, Belgium, Neurology, [6] GHDC, Charleroi, Belgium, Intensive Care, [7] GHDC, Charleroi, Belgium, Gastroenterology.

A 61-year-old woman presented with disabling watery diarrhea, occurring more than 20 times per day for the past two months. She reported no abdominal pain, fever, rectal bleeding nor melena. She experienced anorexia and a 10-kg weight loss. Upper endoscopy revealed antral erythematous gastritis, erosive bulbitis, and erythematous duodenitis. Both *Helicobacter pylori* testing and *Giardia* antigen were negative. Colonoscopy showed petechial right colitis; histology revealed nonspecific inflammation, with suspicion of drug-induced colitis. Given her history of olmesartan use, the drug was discontinued, but no improvement occurred after one month. Only loperamide (2 tablets/day) partially controlled her symptoms. She was then given cholestyramine for one week followed by budesonide, in line with management of microscopic colitis, but without clinical benefit. Hospitalization was required for further evaluation. Abdominal and thoracic CT scans revealed a spiculated pulmonary nodule in the right upper lobe and a suspicious left adrenal mass. Laboratory tests showed markedly elevated chromogranin A (484.2 µg/L), while urinary 5-HIAA and stool studies (steatocrit, faecal elastase) were ordered. Treatment with subcutaneous Siroctid (three injections daily) was initiated. Bronchoscopic biopsies confirmed a neuroendocrine tumour, histologically atypical due to the presence of necrosis. Staging work-up showed diffuse bone marrow hypermetabolism, a left adrenal adenoma, and a nodular appearance of the pituitary gland without underlying lesion. NSE was also elevated (76 µg/L). Further evaluation with an octreotide PET scan and adrenal biopsy were planned to better assess disease extent. Overall, the diagnosis was a carcinoid syndrome secondary to an atypical pulmonary neuroendocrine tumour. The presence of a left adrenal adenoma, a suspected pituitary macroadenoma, and the pulmonary carcinoid tumour also raised concern for multiple endocrine neoplasia type 1 (MEN-1). Unfortunately, the patient was admitted to the intensive care unit with status epilepticus. Brain MRI revealed ischemic lesions as well as bone lesions, likely metastatic. Urinary catecholamines were elevated, but specific metanephrines were negative. Despite multiple therapeutic interventions, she developed recurrent infectious and vascular complications, continued to experience severe refractory diarrhoea, and passed away two months later. Pulmonary carcinoids are rare, low-grade malignant tumours, with an estimated incidence of 0.2 to 2 cases per 100,000 population per year. Carcinoid syndrome is uncommon in pulmonary neuroendocrine tumours, occurring in only 2–5% of cases. The symptoms are related to the secretion of vasoactive substances, mainly serotonin, and typically include flushing, abdominal cramps, and debilitating diarrhoea. Moreover, approximately 5% of bronchial carcinoid tumours are associated with multiple endocrine neoplasia type 1 (MEN1), most of them being of the typical type. Only two similar cases of relentless diarrhoea caused by carcinoid syndrome secondary to a NET have been reported in the literature; however, both described typical carcinoid tumours on histology. Atypical neuroendocrine tumours are even more rare. To our knowledge, this is the first reported case of carcinoid syndrome presenting with chronic diarrhoea caused by an atypical pulmonary neuroendocrine tumour. To conclude, although carcinoid syndrome is an uncommon condition, it remains an important differential diagnosis in patients presenting with unexplained chronic diarrhea. Recognizing this rare syndrome early is essential, as it enables appropriate hormonal assessment, imaging, and therapeutic planning to improve patient outcomes.

-C05-

PORTO-SINUSOIDAL VASCULAR DISEASE IN TWO PATIENTS WITH TAFRO SYNDROME: A CASE SERIES. F. Poletti (1), L. Dassy (2), K. Hafraoui (3), M. Lejeune (4), J. Somja (5), P. Collins (5), J. Guiot (6), J. Caers (2), A. Marot (1), J. Delwaide (7), V. Putzeys (8), G. Vertenoeil (2) / [1] Centre Hospitalier Universitaire Mont-Godinne, Belgium, Gastroenterology and Hepatology, [2] CHU de Liège, Liège, Belgium, Haematology, [3] CHR Verviers, Verviers, Belgium, Haematology, [4] CHR Citadelle, Liège, Belgium,

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Introduction: Porto-sinusoidal vascular disorders (PSVD) are rare hepatic vascular conditions characterized by lesions in the portal venules and hepatic sinusoids, that can cause portal hypertension without liver cirrhosis. Patients are usually asymptomatic until the development of portal hypertension complications. TAFRO syndrome (Thrombocytopenia, Anasarca, Fever, Reticulin fibrosis/Renal insufficiency and Organomegaly) is a rare systemic inflammatory disease that is classified as a subtype of idiopathic multicentric Castelman disease. In this case series, we report two cases of TAFRO syndrome with PSVD.

Cases description: We describe the case of a 57-year-old woman followed since 2012 for progressive fatigue, general decline, abdominal discomfort with bloating, and intermittent lower-limb oedema suggestive of fluid overload. Her medical history was unremarkable, and she was only taking a proton pump inhibitor and an oral contraceptive. The diagnostic workup revealed lymphadenopathy, evidence of inflammatory syndrome and mild cholestasis. Between 2014 and 2016, she progressively developed ascites and hepatosplenomegaly, as well as oesophageal varices with persistent cholestasis but no jaundice. Morphological assessment also revealed recanalization of the umbilical vein, a typical sign of portal hypertension. The liver biopsy showed hepatic peliosis. In 2017, presence of refractory ascites required placement of a TIPS with no clinical improvement thereafter. In 2018, she presented with thrombocytopenia ($27 \times 10^3/\text{mm}^3$), anaemia (9.1 g/dL), and neutropenia ($0.07 \times 10^3/\text{mm}^3$) and progressive cholestasis. A lymph node biopsy revealed florid follicular hyperplasia with interfollicular plasmacytosis, and an increased number of megakaryocytes were observed in the bone marrow. Cyclosporine was initiated but she relapsed with severe thrombocytopenia. Treatment for immune thrombocytopenia (dexamethasone and IVIG) was attempted. In 2019, a TAFRO syndrome was diagnosed according to the Masaki criteria. Tocilizumab, a monoclonal antibody that blocks the function of interleukin-6 (IL-6), led to partial improvement in thrombocytopenia, maintaining it at $\sim 100 \times 10^3/\text{mm}^3$, as well as stabilizing lymphadenopathy and splenomegaly. Complete resolution of inflammatory features, disappearance of ascites and a remarkable improvement in quality of life were also observed.

The second patient, a 68-year-old woman, initially presented in 2024 with isolated thrombocytopenia ($67 \times 10^3/\text{mm}^3$), which was first considered compatible with immune thrombocytopenia. In June 2025, she was hospitalized for a further decline in platelet count ($26 \times 10^3/\text{mm}^3$). Laboratory testing also demonstrated mild cholestasis. Abdominal CT revealed hepatosplenomegaly and features of portal hypertension, including dilation of the extrahepatic portal vein, peri-splenic varices, and splenomegaly. Upper endoscopy confirmed the presence of oesophageal varices. The liver biopsy showed nodular regenerative hyperplasia. Bone marrow aspiration again showed megakaryocytic hyperplasia. Dexamethasone and IVIG were ineffective. Her condition rapidly deteriorated with fever, anasarca, and development of hepatic encephalopathy. TAFRO syndrome was finally diagnosed according to the Masaki criteria. Treatment with corticosteroids and tocilizumab was initiated. Given the absence of clinical and biochemical improvement, a switch to rituximab was required. Despite this therapeutic adjustment, no significant response was observed, and the patient subsequently died shortly thereafter.

Discussion: The coexistence of PSVD and TAFRO syndrome is rarely reported in the literature. In this case series, we present the clinical course and management of two patients with TAFRO syndrome and concomitant PSVD. Both patients exhibited thrombocytopenia, anasarca, systemic inflammation, and organomegaly, as well as evidence of portal vascular abnormalities in liver biopsies. They were treated with a high dose of corticosteroids, followed by tocilizumab. One patient showed partial resolution of thrombocytopenia and normalization of the signs of portal hypertension, with sustained clinical improvement. The other patient developed multiple organ complications, failed to respond to therapy, and ultimately died. These cases highlight the potential association between TAFRO syndrome and PSVD. Early recognition of this rare combination is important for diagnosis, management and prognosis.

-C06-

A RARE CAUSE OF BILIARY OBSTRUCTION - REVISITING THE DIAGNOSIS. P. Clarysse (1) / [1] AZ Sint-Jan Brugge-Oostende, Brugge, Belgium, Gastroenterology.

A 43-year-old patient consulted our hospital after a left hepatectomy performed for retro-obstructive severe dilatation of the intrahepatic bile ducts in the left liver lobe, with a presumed diagnosis of Caroli disease. Postoperatively, the patient experienced recurrent episodes of colicky abdominal pain, night sweats, and weight

loss, in combination with persistently cholestatic liver enzyme abnormalities in the absence of inflammatory markers. Repeat MRCP revealed new obstructive dilatation of the anteromedial bile ducts of the right liver lobe, confirmed by ERCP, which showed significant fibrosis at two branches of the right hepatic duct. The original resection specimen was re-evaluated at our tertiary centre, which led to a revised diagnosis: a granular cell tumour of the bile ducts. Mebrofenin scintigraphy showed adequate residual liver function to allow for further resection. The patient subsequently underwent an extended left hepatectomy with hepaticojejunostomy to remove the remaining affected tissue. Granular cell tumours are rare neoplasms typically originating from Schwann cells. They most commonly occur in the head and neck region, particularly the tongue. Involvement of the biliary tract is exceedingly rare and can lead to significant biliary duct obstruction and dilatation. This case illustrates the diagnostic challenges posed by rare biliary tumours and the potential for initial misclassification. It emphasizes the value of re-evaluating histopathology and integrating advanced imaging when symptoms persist. Recognizing a granular cell tumour in this context can broaden the differential diagnosis of biliary obstruction and provide useful insights for hepatology practice.

-C07-

POST-BYPASS MALNUTRITION TRIGGERING EARLY POST-TRANSPLANT STEATOHEPATITIS: RESOLUTION VIA EUS-GUIDED GASTRO-GASTROSTOMY. E. Grégoire (1), M. Messaoudi (1), P. Baldin (2), E. Danse (3), N. Lanthier (1), O. Ciccarelli (4), E. Dubois (5), P. Deprez (1), G. Dahlqvist (6) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'hépatogastroentérologie, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'anatomopathologie, [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service de radiologie et imagerie médicale, [4] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service de chirurgie abdominale et transplantation, [5] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'alimentation et diététique, [6] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Service d'hépatogastroentérologie.

Liver steatosis is a well-known pathological condition characterized by the accumulation of fat in the liver, most often caused by excessive alcohol consumption or metabolic dysfunction associated steatotic liver disease (MASLD). Bariatric surgery has been proven as an option for reversing MASLD related lesions in patients with severe obesity. With the increasing numbers of patients undergoing gastric bypass surgery, we have observed a phenomenon probably linked to malabsorption and bacterial overgrowth, both leading to a specific phenotype of steatohepatitis, bile duct alteration and portal inflammation. Malnutrition leads to major hepatic steatosis due to insufficient protein absorption, which in turn leads to the cessation of essential metabolic processes and the activation of genes that stimulate lipogenesis. In liver transplant patients, acute steatohepatitis of the graft can be life-threatening.

Here, we present a case of a 52 years-old female patient, followed up for mixed metabolic and alcohol-related (met-ALD) decompensated cirrhosis, Child-Pugh C and MELD 24, complicated by portal hypertension and refractory hydrothorax. The patient has a medical history of obesity and surgical history of Roux-en-Y gastric bypass surgery in 2015. Orthotopic liver transplantation was performed in March 2025, with a graft from a donor after cardiac death. The procedure was completed without surgical complication. The hepatectomy specimen confirms a histopathological appearance consistent with cirrhosis caused by steatohepatitis compatible with a mixed origin (ALD and MASH) without signs of malignancy, with a Beaujon score of S3 A4 F4 and a Metavir fibrosis score of F4. The reperfusion liver biopsy showed a hepatic parenchyma characterized by mild surgical hepatitis with the presence of a few Councilman bodies and very mild focal microvacuolar steatosis (Metavir fibrosis score F0-F1). At discharge, three weeks after surgery, laboratory tests showed AST 36 U/L (N <40), ALT 18 U/L (N <40), GGT 220 U/L (N <50), alkaline phosphatase 252 U/L (N <102) and total bilirubin 0.8 mg/dL. A month later (mid-April 2025), the patient was hospitalized due to abnormal liver tests and refractory ascites. Her lab values showed AST at 140 U/L (N <40), ALT 66 U/L (N <40), GGT 317 U/L (N <50), alkaline phosphatase 745 U/L (N <102) and total bilirubin 2.8 mg/dL (N < 1.2 mg/dl). Biliary complication was ruled-out, and a liver biopsy was performed revealing the presence of MASH-type steatohepatitis and architectural abnormalities of the bile ducts with ductal proliferation and signs of cholestasis. This was consistent with post-bypass malnutrition. Continued alcohol abstinence was confirmed by a negative phosphatidylethanol test, as immunosuppression was well-managed with tacrolimus levels within the target ranges. We attempted to improve oral nutrition with enteral naso-gastric tube, but despite adequate oral and enteral refeeding, there was no improvement in the clinical situation and liver tests remained abnormal. For this reason, in September 2025, an endoscopic gastro-gastrostomy (EDGE) was performed by inserting a 10 x 20 mm HotAxios prosthesis and initiating trans-prosthetic feeding into the

excluded stomach via a nasogastric tube (aiming for an intake of 35 kcal/kg/day with 1.2 g of protein/kg/day). Within six weeks after starting this targeted nutrition, the biological evolution dramatically improved with AST 12 U/L (N <40), ALT 8 U/L (N<40), GGT 30 U/L (N<50), alkaline phosphatase 111 U/L (N<102) and total bilirubin of 0.3 mg/dL. In parallel, interestingly, we observed a marked increase in liver density on CT scan compatible with disappearance of hepatic steatosis.

This case illustrates the diagnostic challenge of acute steatohepatitis related to malnutrition in patients with a history of gastric bypass surgery. Indeed, the paradoxical presence of hepatic steatosis in the setting of severe malnutrition—in patients who are often perceived as being at risk for overweight—frequently delays recognition of the clinical presentation. The risk of early post-liver transplant recurrence of this phenomenon must also be taken into consideration at the time of transplantation. Management is complex. Although nutritional rehabilitation remains the only validated treatment, post-bypass anatomy often limits adequate intake. Options include enteral nutrition via gastric or nasojejunal tubes, the placement of lumen-apposing metal stent (LAMS) to access the excluded stomach, or surgical revision. Surgical reversal is technically demanding and carrying substantial morbidity. EUS-guided placement of a LAMS provides a minimally invasive alternative by creating a gastro-gastric fistula. Partial RYGB reversal using a LAMS may improve nutritional parameters and resolve hepatic steatohepatitis with lower morbidity than surgical revision.

-C08-

DIFFUSE INTRADUCTAL PAPILLARY NEOPLASIA OF THE BILE DUCTS (IPNB) MIMICKING UNRESECTABLE HILAR CHOLANGIOCARCINOMA: THE PIVOTAL ROLE OF CHOLANGIOSCOPY FOR MAPPING AND ORGAN-SPARING MANAGEMENT. H. Couvert (1), Y. Hasnaoui (2), S. Meuree (2), P. Deprez (3), A. Bourgeois (4), D. Bléro (5) / [1] Institut Jules Bordet, Brussels, Belgium, Digestive Oncology, [2] Department of Gastroenterology and GI oncology, Hôpital Erasme, Hôpital Universitaire de Bruxelles, Université Libre de Bruxelles, Brussels, Belgium, Brussels, Belgium, Gastro-entérologie, [3] UCLouvain, Cliniques universitaires Saint-Luc, Belgium, Gastro-entérologie, [4] Clinique Saint-Luc Bouge, Namur, Belgium, Gastro-entérologie, [5] UCL Saint-Luc, Brussels, Belgium, Gastro-entérologie.

Introduction: Intraductal papillary neoplasia of the bile ducts (IPNB) is a rare precancerous condition. Its clinical presentation, often manifesting as an obstructive hilar mass, can mimic perihilar cholangiocarcinoma (Klatskin tumour), creating significant diagnostic and therapeutic challenges. We report a case of diffuse IPNB mimicking an inoperable hilar tumour, illustrating the discrepancy between aggressive imaging and benign histology, and highlighting the crucial role of direct cholangioscopy mapping in guiding radiofrequency ablation (RFA) as an organ-sparing therapy.

Case Report: A 78-year-old female with a history of vasoplegic angina presented with anicteric cholestasis (total bilirubin 1.58 mg/dL, GGT 1491 IU/L), weight loss, and right upper quadrant pain. Initial cross-sectional imaging (CT and MRI) revealed a 45x18 mm bilobed tumour mass in the hepatic hilum with intraluminal invasion extending to the confluence and right secondary ducts, strongly suggestive of a Bismuth type IIIa tumour. Paradoxically, histological evaluation was reassuring. The initial ERCP, complicated by pancreatitis (CTSI 2), allowed for right-sided stenting but failed on the left; blind biopsies only revealed a papillary tumour with low-grade dysplasia. Due to this discordance, endoscopic ultrasound (EUS) was performed, visualizing a soft, purely intraluminal oblong lesion (4x2 cm, uT1). EUS-guided biopsies showed no signs of malignancy. However, an FDG PET-CT confirmed focal hilar hypermetabolism. Faced with this diagnostic impasse and the patient's reluctance regarding major surgery, direct cholangioscopy (SpyGlass) was performed. It rectified the diagnosis by revealing diffuse papillomatosis (appearing as a "villous carpet") extending from the common hepatic duct to the bilateral secondary convergences, reclassifying the lesion as Klatskin IV, with additional focal lesions in the lower common bile duct and perihilar region. This direct visualization, combined with pathological findings, confirmed diffuse IPNB. Consequently, scheduled endobiliary radiofrequency ablation (RFA) was selected, favoring local control over mutilating or unfeasible surgery. **Discussion:** This case underscores the complexity of extensive IPNB. Firstly, the exophytic growth of IPNB can mimic invasive cancer on imaging, leading to radiological-pathological discordance and underestimation of disease extent. Secondly, direct visualization is mandatory for accurate mapping. In this case, the use of cholangioscopy transformed the staging from Bismuth IIIa (theoretically resectable via extended right hepatectomy) to a diffuse stage IV, radically altering management. Finally, in frail patients with diffuse disease (Klatskin IV), intracanalicular RFA is emerging as a new and viable alternative to liver transplantation or therapeutic abstention. Recent data suggest RFA may offer effective biliary patency control and prolonged survival in non-invasive or locally advanced IPNB.

Conclusion: In cases of tumour-like hilar obstruction with discordant benign biopsies, IPNB must be considered. This case demonstrates that cholangioscopy is essential not only for histological confirmation but, more importantly, for pre-treatment mapping. It allows inoperable or high-risk patients to be referred for innovative endoscopic therapies such as radiofrequency ablation, offering new prospects for organ preservation.

-C09-

CYTOMEGALOVIRUS-ASSOCIATED MENETRIER'S DISEASE IN A 3-YEAR-OLD CHILD: A RARE CAUSE OF ACUTE PROTEIN-LOSING GASTROPATHY. C. Schoonbroodt (1), M. Leonard (2), A. Lhomme (2), L. D'Angelo (2), L. Zambelli (2), F. Chalon (2), J. Frère (3), V. Fridman (4), E. Bequet (2) / [1] CHR Citadelle, Liège, Belgium, Pédiatrie, [2] CHR Citadelle, Liège, Belgium, Gastro-pédiatrie, [3] CHR Citadelle, Liège, Belgium, Infectiologie pédiatrique, [4] CHR Citadelle, Liège, Belgium, Anatomopathologie.

Menetrier's disease is a rare hypertrophic gastropathy leading to protein-losing gastropathy and is associated with cytomegalovirus (CMV) infection in approximately 70% of paediatric cases. It should be considered in any child presenting with acute-onset hypoalbuminemia and oedema, suggestive of protein loss from the gastrointestinal tract. In most paediatric cases, protein-losing disorders arise from enteric pathology involving the small bowel or colon, while gastric protein leakage is distinctly uncommon. This distinction is clinically relevant, as it shapes the initial diagnostic approach: evaluation typically targets the lower gastrointestinal tract, making the identification of a gastric cause—such as Menetrier's disease—unexpected. Although generally transient and with a favourable outcome in children, this condition requires early recognition to ensure timely and appropriate management. In severe cases, particularly when active CMV infection is confirmed, targeted antiviral therapy may accelerate recovery and help prevent complications.

A 3-year-5-month-old boy presents with progressive facial, limb, and scrotal oedema in a context of abdominal pain evolving for two weeks. Laboratory tests show global hypoproteinaemia (2.8 g/dL), severe hypoalbuminemia (1.8 g/dL), and global hypogammaglobulinemia, without inflammatory response or hepatic dysfunction. Urinary protein loss is excluded and cardiac evaluation is normal. The laboratory workup also shows iron deficiency and vitamin B12 deficiency, without other significant micronutrient abnormalities. Ileo-colonoscopy shows no abnormalities. In contrast, upper gastrointestinal endoscopy reveals a thickened, haemorrhagic, polypoid gastric mucosa with a characteristic “cushion-like” appearance. Histology demonstrates foveolar hyperplasia, marked mucosal oedema, and a dense eosinophilic infiltrate. *Helicobacter pylori* infection is ruled out. Active CMV infection is confirmed by positive serology and by CMV PCR in both blood and gastric biopsies. Management includes albumin infusions, diuretics, short-course corticosteroids, and nutritional support. Given the severity of protein loss and the confirmed CMV infection, intravenous ganciclovir is administered for two weeks, followed by oral valganciclovir for a total antiviral duration of two months. The clinical course is favourable, with resolution of oedema and normalization of serum proteins within three weeks. At one month, follow-up gastroscopy shows near-complete mucosal healing, and CMV PCR becomes negative.

This case highlights the importance of considering CMV-associated Menetrier's disease in children presenting with rapidly developing hypoalbuminemia and oedema of digestive origin. While most paediatric cases resolve spontaneously, severe forms with confirmed active CMV infection may benefit from antiviral therapy, potentially accelerating recovery and preventing complications.

-C10-

WHEN DIFFUSE LYMPHADENOPATHIES MIMIC LYMPHOMA: A DIAGNOSTIC PITFALL. A. Hassine (1), L. Triki (1), M. Ilzkovitz (2), M. Pezzullo (3), P. Eisendrath (4), C. Maris (5), M. Arvanitakis (1), M. Fernandez Y Viesca (1) / [1] Erasme Hospital, Brussels, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, Hôpital Universitaire de Bruxelles, Université Libre de Bruxelles, Brussels, Belgium, [2] Erasme Hospital, Brussels, Belgium, Department of Internal Medicine, Hôpital Universitaire de Bruxelles, Université Libre de Bruxelles, Brussels, Belgium, [3] Erasme Hospital, Brussels, Belgium, Department of Radiology, Hôpital Universitaire de Bruxelles, Université Libre de Bruxelles, Brussels, Belgium, [4] CHU Saint-Pierre, Brussels, Belgium, Department of Gastroenterology, CHU Saint-Pierre, Brussels, Belgium., [5] Erasme Hospital, Brussels, Belgium, Pathology Department, Hôpital Universitaire de Bruxelles, Université Libre de Bruxelles, Brussels, Belgium.

Introduction: Whipple's disease, caused by *Tropheryma whipplei*, is a rare multisystem infection. Although classically presenting with malabsorption or arthralgia, atypical or misleading manifestations may closely mimic hematologic disorders, leading to significant diagnostic delay. Accurate diagnosis requires the combination of clinical, biochemical, imaging, histologic, and molecular findings. We report a case of Whipple's disease in which diffuse lymphadenopathies and a marked inflammatory syndrome initially raised high concern for a lymphoproliferative disease.

Case Description: A 39-year-old woman with perinatal hypoxic brain injury was referred for persistent systemic inflammation associated with chronic peri-umbilical pain, vomiting, constipation, and a 20 kg weight loss over two years. Laboratory investigations demonstrated CRP up to 120 mg/L, ESR 115 mm/h, polyclonal hypergammaglobulinemia, elevated vitamin B12, low folate. Autoimmune work-up showed an elevated rheumatoid factor, while anti-CCP was negative and C3/C4 levels were within normal range. Infectious work-up including blood cultures and Quantiferon® was negative. CT and PET-CT revealed multiple supraclavicular, mediastinal, mesenteric, and retroperitoneal lymphadenopathies, bulky, confluent, and low-density on CT—with intense hypermetabolic activity (SUV max 6–11), including focal uptake in the right colon and ileum. These findings strongly suggested a lymphoma. Peripheral blood immunophenotyping identified a monoclonal B-cell population compatible with marginal zone lymphoma, reinforcing the suspicion of a lymphoproliferative disorder. Ileo-colonoscopy and supraclavicular lymph node biopsy were unremarkable. EUS demonstrated a cluster of hyperechoic retroperitoneal mesenteric lymph nodes, the largest measuring 2 cm near the SMV, which was sampled using FNB (five passes). Endoscopy revealed a brownish, atrophic duodenal mucosa with suspected lymphoid infiltration. Duodenal biopsies and lymph node FNB revealed numerous PAS- and PAS- diastase-positive macrophages. Molecular analysis and PCR performed on paraffin-embedded material was positive for *Tropheryma whipplei*, confirming disseminated Whipple's disease. After PCR confirmation, the patient was initiated on intravenous ceftriaxone for 14 days, followed by long-term oral doxycycline planned for 12 to 24 months in accordance with therapeutic recommendations for Whipple's disease.

Conclusion: This case illustrates an uncommon presentation of Whipple's disease mimicking lymphoma and underlines the important role of endoscopy providing histology and PCR testing for *Tropheryma whipplei* in unexplained systemic inflammation and atypical lymphadenopathy.

**BELGIAN SOCIETY FOR GASTROINTESTINAL ENDOSCOPY (BSGIE)
- THURSDAY SESSION**

-G01-

IMPROVING CELLULAR YIELD DURING ENDOSCOPIC BRUSH SAMPLING BY NOT RESHEATHING - A SIMPLE MODIFICATION. M. Wyckmans (1), A. Driessen (2), S. Krishnadath (1) / [1] Antwerp University Hospital, Edegem, Belgium, Gastroenterology and Hepatology, [2] Antwerp University Hospital, Edegem, Belgium, Pathology.

Introduction: Brush cytology allows sampling of broad mucosal areas. It has various gastrointestinal indications such as malignancy, Barrett's oesophagus and Helicobacter pylori infection. During endoscopy, the brush bristles exit a protective sheath. After sampling, the bristles retract back into the sheath. While few studies have explored the role of the plastic sheath on cellularity, loss of cellularity during sheath retraction is observed in the literature.[1, 2] Research on behalf of ENDEAVOR consortium (<https://endeavoreu.com/>), funded by the EU Horizon Grant 101136935.

Aim: As diagnostic accuracy depends on cellularity yield, this study investigated whether not retracting the bristles into the sheath is feasible and results in better cellular yield and diagnostic accuracy.

Methods: Patients with Barrett oesophagus undergoing standard-of-care endoscopy were included at the Antwerp University Hospital. Endoscopy was performed by two experienced gastroenterologists. Brush samples were taken with either 'standard-of-care' brush retraction (=control) or 'unsheathed' (=intervention). The modified technique has been filmed in a stepwise manner for standardisation and training purposes. Samples were stored in Cytolyt cell medium and directly transported to the department of Pathology for cytological evaluation and formalin-fixation for cellblock. Cellularity results were defined as 'insufficient', 'low', 'moderate' and 'high'. [3] Cellularity results were bundled in two groups 'insufficient-to-low' and 'moderate-to-high' in order to facilitate statistical analysis using Fisher's exact test at 95% confidence interval. Diagnostic accuracy was evaluated whether the brush cytology could confirm diagnosis of Barrett oesophagus.

Results: 17 patients with Barrett oesophagus were included during a one-year period for a total of 32 brush samples. When brush retraction was performed, cellularity was insufficient-to-low in 47.4% (9 brushes) and moderate-to-high in 52.6% (10 brushes). When the unsheathed technique was used, cellularity was moderate-to-high in 100% (13 brushes). There were no brushes that yielded insufficient-to-low cellularity. When comparing the two techniques, there is more cellular yield when not retracting ($p = 0.0042$). Diagnostic accuracy was 52.6% when brush retraction was performed, while diagnostic accuracy increased to 61.5% with the unsheathed technique. This result was not statistically significant (p -value 0.72).

Conclusions: This small-scale study points out better cellular yield by not retracting the brush into the sheath during endoscopic brush sampling. A larger sample size is needed to confirm the benefit in diagnostic accuracy. The modified technique is promising and further research can determine whether these findings can be applied for other indications of brush cytology. As part of the Horizon Europe Project ENDEAVOR, endoscopic brush samples will be taken between abstract submission and presentation from multiple international sites trained in the technique. These results will allow evaluation of replicability and performance in a population with Barrett oesophagus high-grade dysplasia and T1 adenocarcinoma.

-G02-

BARRETT'S OESOPHAGUS WITH LOW GRADE DYSPLASIA : IMPACT OF EXPERT HISTOPATHOLOGICAL REVIEW AND EXPERT ENDOSCOPIC REASSESSMENT ON ONCOLOGICAL STAGING: A RETROSPECTIVE BICENTRIC BELGIAN STUDY. G. Bastens (1), L. Verset (2), N. Blétard (3), O. Plomteux (4), P. Eisendrath (5), P. Leclercq (4), A. Lemmers (6) / [1] CHC, Liège, Belgium, Gastroenterology, [2] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Pathology, [3] Clinique MontLegia - CHC Groupe Santé, Liège, Belgium, Pathology, [4] Clinique MontLégia- CHC Groupe Santé, Liège, Belgium, Gastroenterology, [5] CHU Saint-Pierre, Brussels, Belgium, Gastroenterology, [6] Department of Gastroenterology and GI oncology, Hôpital Erasme, Hôpital Universitaire de Bruxelles, Université Libre de Bruxelles, Brussels, Belgium, Brussels, Belgium, Gastroenterology.

Introduction: Barrett's oesophagus (BE) represents a well-established risk factor for esophageal adenocarcinoma (EAC), which typically arises through a sequence of histological changes from non-dysplastic BE (NDBE) to low grade dysplasia (LGD), high grade dysplasia (HGD), and carcinoma. Although the annual progression rate from NDBE is relatively low, the prognosis of EAC remains poor, underscoring the importance

of early detection and accurate risk stratification of dysplastic lesions. LGD in BE carries a heterogeneous risk of progression and substantial diagnostic variability. Previous studies have shown that up to 85% of LGD diagnoses made in community settings are downgraded to NDBE or indefinite for dysplasia (IND) after expert panel review. In contrast, when LGD is confirmed by a panel of at least two expert pathologists, the risk of progression rises sharply. Additionally, patients should undergo restaging endoscopy at a specialized centre, using high-definition imaging, acetic acid or virtual chromoendoscopy, and meticulous inspection to detect visible lesions. Previous multicentre data have shown that expert endoscopic restaging significantly altered patient management, with 25% of the patients ultimately reclassified as having HGD or EAC. Expert histopathological review and expert endoscopic reassessment are recommended by international guidelines, but their real-world practice implementation added value requires further studies.

Aim: To evaluate the diagnostic impact of expert histopathological review and expert endoscopic restaging in patients with LGD managed in two Belgian expert centres.

Methods: We conducted a retrospective bicentric cohort study across two Belgian BE expert centres including all endotherapy-naïve patients with at least one diagnosis of LGD between January 2018 and December 2024 and at least one follow-up endoscopy. Data were extracted from electronic endoscopy and pathology records and manually validated. Patients with prior HGD, EAC, IND or previous endoscopic therapy were excluded. Three main subcohorts were defined: (1) a Histopathology Review Cohort, including patients whose LGD biopsies underwent expert gastrointestinal (GI) pathology review; (2) an Expert Endoscopy Cohort, including patients referred for LGD restaging by a Barrett's expert endoscopist; and (3) a Combined Expert Cohort, including patients who underwent both expert histology review and expert endoscopy. Primary outcomes were (1) diagnostic reclassification after expert histopathological review and (2) detection of visible lesions and histologic outcomes at the first expert endoscopy. The secondary outcome was the diagnostic concordance and clinical impact of combined expert histological and endoscopic reassessment. Only descriptive statistics were performed.

Results: A total of 148 patients with a diagnosis of LGD in the context of BE were included. Median age was 67 years and 79.7% were male. The median Prague classification was C1M4. Expert histopathology review was performed in 107/148 patients (72.8%). A diagnostic change occurred in 27 cases (25.2%). LGD was confirmed in 80 patients (74.8%). Among reclassified case, 10 (9.3%) were upgraded to HGD and 17 (15.9%) were downgraded (14 to IND, 3 to NDBE). Expert endoscopic reassessment was performed in 85 patients referred specifically for LGD evaluation; 79 were included after excluding 6 upgraded to HGD on expert pathology review. At the first expert endoscopy, histologic outcomes were: HGD/EAC in 11 patients (13.9%), persistent LGD in 26 (32.9%), IND in 6 (7.6%) and NDBE in 36 (45.5%). A visible lesion was identified in 18/79 patients (22.8%). The combined expert cohort (patients with expert-confirmed LGD undergoing expert endoscopy) included 62 patients. In this group, first expert endoscopy revealed HGD/EAC in 15 (24.2%), persistent LGD in 24 (38.7%), IND in 6 (9.7%) and NDBE in 17 (27.4%). Among 10 patients whose LGD was not confirmed by expert pathology, none showed dysplasia on expert endoscopy. Overall, expert pathological review and expert endoscopic restaging led to substantial diagnostic reclassification, frequently identifying previously unrecognized visible lesions and higher-grade neoplasia.

Conclusions: LGD in BE requires cautious management given its diagnostic variability. Our findings align with international series in demonstrating the critical role of expert histopathology review and expert endoscopy to confirm the diagnosis, detecting missed visible lesions and guiding the appropriate therapy. These results support systematic referral of all patients with suspected or confirmed LGD to expert centres before any therapeutic decision.

-G03-

BELGIAN BARRETT'S OESOPHAGUS RFA REGISTRY: IMPROVED EFFICACY AND MAINTAINED SAFETY AFTER REIMBURSEMENT-DRIVEN CENTRALIZATION. P. Leclercq (1), D. Tate (2), P. Deprez (3), D. De Wulf (4), A. Lemmers (5), P. Eisendrath (6), S. Van Langendonck (7), P. Dewint (8), M. Bronswijk (9), C. Snauwaert (10), M. Poncin (11), A. Badaoui (12), C. Camps (13), H. Willekens (13), R. Bisschops (13) / [1] Clinique MontLégia; CHC Groupe Santé, Liège, Belgium, Gastroenterology, [2] Ghent University Hospital, Ghent, Belgium, Gastroenterology and Hepatology, [3] UCL Saint-Luc, Brussels, Belgium, Gastroenterology and Hepatology, [4] AZ Delta, Belgium, Gastroenterology and Hepatology, [5] H.U.B - CUB Hôpital Erasme, Brussels, Belgium, Gastroenterology and Hepatology, [6] CHU Saint-Pierre, Brussels, Belgium, Gastroenterology and Hepatology, [7] AZ Maria Middelaes, Ghent, Belgium, Gastroenterology and Hepatology, [8] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology and Hepatology, [9] Imelda Hospital, Bonheiden, Belgium, Gastroenterology and Hepatology, [10] AZ Sint-Jan Brugge-Oostende, Brugge, Belgium, Gastroenterology and Hepatology, [11] CHU de Liège, Liège, Belgium,

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Introduction: Volume expansion following reimbursement of advanced procedures typically raises concerns about quality dilution, particularly when techniques disseminate beyond specialized centres. This prospective Belgian registry investigated whether national reimbursement for radiofrequency ablation (RFA) of Barrett's oesophagus affected treatment outcomes, comparing two 7-year periods before and after reimbursement implementation (2010–2016 vs 2017–2023) across 12 designated expert centres.

Aim: We assessed changes in case volume, patient characteristics, treatment patterns, efficacy, and safety.

Methods: Patients were allocated according to their first RFA procedure into prereimbursement (2010–2016) and post-reimbursement (2017–2023) cohorts. Variables included demographics, Prague C/M classification, worst pre-RFA histology, pre-RFA endoscopic resection (ER), number of RFA sessions, efficacy outcomes (complete eradication of intestinal metaplasia [CE-IM], complete eradication of dysplasia [CE-D]), and adverse events. Efficacy required ≥ 1 surveillance biopsy within 12 months after final RFA. Statistical comparisons used chi-square or Fisher's exact tests for categorical variables and Mann–Whitney U tests for continuous variables.

Results: RFA case volume increased 71% following reimbursement (345 vs 589 patients, $p < 0.001$). Post-reimbursement patients presented with shorter Barrett's segments (Prague C: 3 vs 2, $p = 0.039$; M: 5 vs 4, $p = 0.031$) and lower HGIN prevalence (62% vs 55%, $p = 0.024$). Contrary to concerns about quality dilution, efficacy improved significantly (CE-IM: 83.1% vs 87.5%, $p = 0.048$), with a strong trend for CE-D (94.0% vs 96.5%, $p = 0.079$), despite higher volumes. Median RFA sessions remained unchanged (2, $p = 0.052$). Safety profiles were excellent and equivalent: bleeding (5% vs 6%, $p = 0.62$), stenosis (9% vs 8%, $p = 0.71$), with zero RFA-related perforations in either period.

Conclusions: This registry reveals a counter-intuitive finding: RFA efficacy improved significantly despite 71% volume expansion following reimbursement. The combination of centralized delivery to expert centres and earlier-stage disease at presentation (shorter segments) appears to have enhanced outcomes rather than diluted them. These data challenge assumptions about volume-quality trade-offs in advanced endoscopic procedures and demonstrate that strategic reimbursement policies coupled with centralization can simultaneously expand access and improve treatment efficacy.

-G04-

THE EFFECTIVENESS OF A HAEMOSTATIC GEL (3D-MATRIX 621-062) IN THE PREVENTION OF DELAYED BLEEDING AFTER EMR OF NON-AMPULLARY DUODENAL LESIONS. S. Arnaert (1), P. Dewint (2), D. De Wulf (3), S. Bouhadan (4), F. Baldaque Silva (5), R. Bisschops (1), I. Demedts (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [2] AZ Maria Middelaers, Ghent, Belgium, Gastroenterology, [3] AZ Delta, Belgium, Gastroenterology, [4] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology, [5] Hospital Pedro Hispano, Matosinhos, Portugal, Gastroenterology.

Introduction: Duodenal endoscopic mucosal resection (EMR) has a high risk of bleeding. In a historical consecutive series of duodenal EMR in our hospital we found in 13/34 cases (38%) active bleeding or high-risk stigma of bleeding (visible vessel after removal of a blood clot) on next day gastroscopy (EGD). Prophylactic application of a haemostatic gel (3D-Matrix 621-062) to the EMR field may be an easy way to prevent delayed bleeding.

Aim: The aim of the study was to assess the efficacy of 3D-Matrix 621-062 in reducing delayed bleeding following duodenal EMR.

Methods: We conducted a single-arm, multicentre observational trial of patients undergoing hot-snare EMR of duodenal non-ampullary lesions of ≥ 10 mm. Following EMR, 3D-Matrix 621-062 was applied directly to the EMR defect. The next day, an EGD was performed to detect active bleeding or high-risk stigma of bleeding (visible vessel after removal of a blood clot). We hypothesized a 50% decrease in bleeding stigma from 38 to 19%; sample size was calculated for power of 90% and Alpha of 0.05. The number of subjects to be enrolled was 59 patients.

Results: From October 2020 until August 2025, 59 patients from 5 different centres were included. Mean lesion size was 21.73 mm. 3D-Matrix 621-062 application was feasible in all patients. On EGD the next day, active bleeding (10 patients; 17%) or visible vessel after removal of a blood clot (6 patients; 10%)

was seen in 16 patients (27%) (Fisher's exact $P=0.35$, NS). During hospital stay, melena and hematemesis were observed in respectively 4 (7%) and 1 patient (2%). Hypotension was not observed. Treatment by placement of a hemoclip was performed in only 9 patients (15%) and relevant blood loss of ≥ 1 g/dL was seen in 3 patients (5%).

Conclusions: Application of 3D-Matrix 621-062 following duodenal EMR did not significantly decrease the rate of bleeding or bleeding stigmata on next day EGD in comparison to a historical cohort.

-G05-

DISSECTION USING PRECISESECT IS FASTER, WITH LESS NEED FOR HAEMOSTATIC GRASPER COMPARED TO SWIFT COAG DURING ESD. I. Cherkaoui-El Fassi (1), M. Figueiredo Ferreira (2), A.M. Bucalau (2), V. Huberty (2), A. Lemmers (2) / [1] Erasme Hospital, Brussels, Belgium, Gastroenterology, [2] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology.

Introduction: Endoscopic Submucosal Dissection (ESD) has become a standard to remove early neoplastic lesions of the GI tract. Technical limits like procedure duration and bleeding management still require improvement. Recently, a new electrosurgical dissection mode (PreciseSect) using dynamic current modulation based on tissue impedance was introduced to enhance haemostasis with less tissue injury. To date, no data compare it with conventional modes such as SwiftCoag.

Aim: This study aimed to compare the SwiftCoag and PreciseSECT modes used during the submucosal dissection step of ESD. Primary outcomes included dissection speed, procedure duration, and use of haemostatic forceps. Secondary outcomes focused on safety through analysis of intra- and post-procedural complications, and pathological specimen quality based on clean margin status

Methods: We conducted a retrospective, single-centre study at a tertiary University Referral Centre. Patients were identified from a prospectively collected registry of ESD procedures performed between 2017 and 2024 using either the SwiftCoag or PreciseSECT electrosurgical modes for the submucosal dissection step of ESD. To ensure maximal standardization, only procedures performed with a Dual Knife-J and glycerol submucosal injection were included. Clinical, procedural, and histopathological data were extracted from electronic records and operative reports. Quantitative variables were analysed using the Mann-Whitney U test, and qualitative variables with Fisher's exact test. Statistical analyses were performed using Jamovi.

Results: Based on the selection criteria, a total of 219 patients were included in the analysis. The study population was composed of 63% men and 37% women, with a median age of 68 (IQR 60.5-74) years. As for the electrosurgical mode used, 146 patients underwent ESD with SwiftCoag and 73 with PreciseSECT. Regarding the anatomical distribution of ESD procedures, 78 were performed in the oesophagus (35.6%), 46 in the stomach (21.0%), 20 in the colon (9.1%), and 75 in the rectum (34.2%). No duodenal procedures were included in the study. There was no significant difference in the anatomical distribution of ESD procedures between the SwiftCoag and PreciseSECT groups. Median procedure duration per ESD was significantly shorter with PreciseSECT (70 min [IQR: 50-90]) compared to SwiftCoag (90 min [IQR: 60-136]; $p = 0.009$). Dissection speed was significantly higher with PreciseSECT (21.2 mm²/min [IQR: 16.17-28.9]) than with SwiftCoag (13.5 mm²/min [IQR: 8.03-20.8]; $p < 0.001$). Use of haemostatic forceps was more frequent with SwiftCoag (69.9%) than with PreciseSECT (54.8%; $p = 0.035$), suggesting improved intraprocedural haemostasis with PreciseSECT. No difference in muscular layer injuries or full-thickness perforations was observed between the SwiftCoag and PreciseSECT groups ($p = 0.098$), the rate of uneventful procedures tended to be higher with PreciseSECT (80.8%) than with SwiftCoag (69.9%), though not statistically significant. Symptomatic esophageal strictures requiring balloon dilation occurring within 90 days after ESD, were observed in 11.5% of patients treated with PreciseSECT and 5.8% with SwiftCoag ($p = 0.394$), suggesting no significant difference in clinical stricture rates. This trend may be partly explained by a higher proportion of extensive resections exceeding 90% of the oesophageal circumference in the PreciseSECT group (34.6% vs 9.6%). Thirty days delayed post-procedural bleeding, was observed in colorectal procedures only. It affected 8.4% of patients overall, with a rate of 15.2% in the PreciseSECT group and 4.8% in the SwiftCoag group ($p = 0.121$). Quality of the specimen was comparable between groups, as reflected by similar en bloc resection rate (93.2% with PreciseSECT; 95.2% with SwiftCoag, $p = 0.540$), clear vertical margin (VM0) rate (97.3% with PreciseSect vs 93.8% with SwiftCoag), $p = 0.079$), clear horizontal margin (HM0) rate (91.8% with PreciSect vs 88.4% with SwiftCoag, $p = 0.626$). Oncologically, low-risk resections, based on ESGE recommendations, were similar

in both groups (PreciseSECT (82.2%) ; SwiftCoag (78.1%) ; $p = 0.222$).

Conclusions: PreciseSECT was associated with faster dissection and less use of haemostatic forceps, with similar en-bloc and margin-free rates compared to SwiftCoag. Our data support PreciseSECT as a facilitating and economical technical improvement of ESD.

-G06-

FEASIBILITY OF DIFFERENTIATING SERRATED PATHWAY POLYPS (GCHP, MVHP AND SSL) BASED ON ENDOSCOPIC APPEARANCE USING DEEP LEARNING. B. Callaerts (1), A. Jans (2), P. Sinonquel (2), X. Sagaert (3), I. Demedts (2), P. Roelandt (2), T. Eelbode (1), S. Tejpar (2), F. Maes (1), R. Bisschops (2) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Electrical Engineering (ESAT/PSI), [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Pathology.

Introduction: Recent molecular studies have suggested a biological link between hyperplastic polyps (HPs) and sessile serrated lesions (SSLs), as early serrated features and BRAFV600E-mutations are frequently found in specific HP subtypes: goblet cell-rich HPs (GCHPs) and microvesicular HPs (MVHPs). This supports the hypothesis that GCHPs, MVHPs and SSLs belong to the serrated neoplasia pathway. **Aim:** In previous work, we demonstrated that deep learning can differentiate GCHPs from MVHPs based on their endoscopic appearance. The present study builds further on this finding by investigating whether deep learning can also distinguish GCHPs, MVHPs and SSLs.

Methods: High-quality white light and i-scan virtual chromoendoscopy videos of polyps, acquired in our centre with Pentax EC38-i20c and EC34-i10 endoscopes, were retrospectively collected, together with their histopathological analysis. Expert pathologists reviewed all cases and reclassified HPs into GCHPs and MVHPs, resulting in a dataset of 260 polyps from 194 patients: 138 GCHPs, 54 MVHPs, and 68 SSLs. The dataset was split into training (70%), validation (10%) and test (20%) sets. Three binary classifiers (GCHP vs MVHP, GCHP vs SSL and MVHP vs SSL) and one ternary classifier (GCHP vs MVHP vs SSL) were trained identically using an EfficientNet B0 backbone with a single video frame as input. Oversampling was applied to balance underrepresented classes. When applying these models to the test cases, predictions for different video frames were aggregated using majority voting.

Results: The test set contained 28 GCHPs, 14 MVHPs and 15 SSLs. The binary GCHP-MVHP model scored 82.7% AUC and 71.4% sensitivity for both classes. The GCHP-SSL model performed similarly with 82.1% AUC and sensitivities of 64.3% and 86.7% for GCHP and SSL respectively. The MVHP-SSL model achieved the highest performance with 87.6% AUC and sensitivities of 71.4% and 80% for MVHP and SSL respectively. In contrast, the ternary model yielded sensitivities of 25%, 64.3% and 60% for GCHP, MVHP and SSL respectively, with GCHP mostly misclassified as MVHP and SSL as GCHP.

Conclusions: Our findings demonstrate that deep learning can differentiate GCHPs, MVHPs and SSLs based on their endoscopic appearance using binary models. The consistently high sensitivity for SSL across the binary models suggests that SSLs have more distinct endoscopic features while differences between GCHP and MVHP are more subtle. The ternary model struggled to reliably discriminate the three classes directly, likely due to the complexity of the task and the limited dataset used. Overall, this study highlights the potential of AI to support endoscopists in recognizing a broader spectrum of serrated polyp types, further enhancing diagnostic precision.

-G07-

ACUTE POST-TRANSPLANT STEATOHEPATITIS IN A PATIENT WITH PRIOR ROUX-EN-Y GASTRIC BYPASS SUCCESSFULLY TREATED BY EDGE PROCEDURE. P. Deprez (1), E. Grégoire (2), M. Messaoudi (2), P. Baldin (3), E. Danse (4), O. Ciccarelli (5), G. Dahlqvist (2) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Gastroenterology, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Hepatogastroenterology, [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Pathology, [4] Cliniques universitaires Saint-Luc, Brussels, Belgium, Radiology, [5] Cliniques universitaires Saint-Luc, Brussels, Belgium, Abdominal surgery and transplantation.

Introduction: With the rising number of gastric bypass procedures, a distinct phenotype of steatohepatitis has emerged, driven by malabsorption and bacterial overgrowth. Severe protein-calorie malnutrition may lead to profound hepatic steatosis by impairing essential metabolic pathways and promoting lipogenesis. In liver transplant recipients, acute steatohepatitis of the graft can be life-threatening.

Aim: To describe a case of post-liver transplantation steatohepatitis related to malnutrition in a patient with prior Roux-en-Y gastric bypass, successfully managed through endoscopic jejuno-gastrostomy (EDGE).

Methods: The patient, previously treated with a Roux-en-Y gastric bypass, received a DCD graft in March 2025 without immediate complications. Initial postoperative liver biopsy showed only mild surgical hepatitis and minimal microvacuolar steatosis. Laboratory values at discharge were near normal except for cholestatic enzymes. One month later, she was rehospitalized for abnormal liver tests and refractory ascites (AST at 140 U/L (N <40), ALT 66 U/L (N<40), GGT 317 U/L (N<50), Alkaline Phosphatase 745 U/L (N<102) and total bilirubin 2.8 mg/dL). Liver biopsy revealed MASH-type steatohepatitis with bile duct abnormalities and cholestasis consistent with malnutrition in the context of bypass anatomy. Alcohol relapse was excluded and immunosuppression remained stable. Attempts to improve nutrition through oral intake and nasogastric enteral feeding were unsuccessful, with persistent biochemical deterioration.

Results: In September 2025, an endoscopic jejuno-gastrostomy (EDGE) was performed using a 10 × 20 mm HotAxios stent to restore access to the excluded stomach and allow targeted nutritional rehabilitation by delivering enteral feeding directly into the excluded stomach via a nasogastric tube. Within six weeks, liver tests normalized (AST 12 U/L, ALT 8 U/L, GGT 30 U/L, ALP 111 U/L, bilirubin 0.3 mg/dL), and abdominal CT demonstrated marked reduction in hepatic steatosis.

Conclusions: This case highlights the diagnostic difficulty of acute steatohepatitis induced by protein-calorie malnutrition in patients with prior gastric bypass, where the paradox of severe steatosis in a malnourished, previously obese patient often delays recognition. Management is challenging because post-bypass anatomy limits adequate nutritional intake. The EDGE procedure, a safe and low-morbidity intervention, offers an effective means of restoring access to the excluded stomach and should be favoured in frail post-transplant patients requiring nutritional optimization.

-G08-

INDICATIONS AND OUTCOME OF ENDOSCOPIC ULTRASOUND-GUIDED CHOLEDOCHODUODENOSTOMY WITH LUMEN-APPPOSING METAL STENTS (LAMSS) IN A TERTIARY REFERRAL CENTRE. M. Nollé (1), P. Hindryckx (2) / [1] Universiteit Gent, Gent, Belgium, medicine, [2] Ghent University Hospital, Gent, Belgium, Gastroenterology.

Introduction: Endoscopic ultrasound (EUS)-guided choledochoduodenostomy (EUS-CDS) using lumen-apposing metal stents (LAMSS) has become an established biliary drainage modality for (malignant) distal biliary obstruction, with or without preceding failed endoscopic retrograde cholangiopancreatography (ERCP). However, previous literature reported a substantial primary and secondary failure rate when using LAMS. The possible reasons for this failure rate or contributing factors behind the primary and secondary outcomes remain incompletely understood and therefore require in-depth investigation.

Aim: A retrospective single-centre analysis in a high-volume tertiary centre was performed to assess the rate of primary and secondary failure of EUS-CDS, and identify potential predictive factors for this failure.

Methods: We collected data from all consecutive patients who had received EUS-CDS with a LAMS (Hot Axios 8/6, Boston Scientific) over the past 5 years at our unit. Demographic, procedural and outcome parameters were carefully captured in a predefined data extraction table. Primary clinical failure was defined as the lack of a $\geq 50\%$ drop in serum bilirubin within 1 week after EUS-CDS. Secondary failure was defined as failure after initial clinical success, necessitating reintervention.

Results: A total of 88 patients were included in the analysis. The mean age was 71 years, with an almost equal male/female ratio (47/41). The vast majority of them received EUS-CDS for malignant distal biliary obstruction, either in a neoadjuvant (N=35, 39.8%) or a palliative (N=40, 45.4%) setting. Six patients (6.8%) were drained with EUS-CDS in the context of benign distal biliary obstruction. The preprocedural common bile duct diameter ranged from 10 to 24 mm. In all patients, a 6/8 LAMS was used (Hot Axios, Boston scientific). LAMS maldeployment took place in 2 patients (2.3%), who had a bile duct diameter of 11mm and 12mm, respectively. The angle between the LAMS axis and the axis of the upstream common bile duct varied from less than 60° to more than 130°. A coaxial double pigtail was placed in only 15 cases (17%). The median follow-up time after LAMS placement was 123 days (range 2-1992 days). The rate of primary stent failure was 11.5%. Evidence of an upstream duodenal substenosis was present in 80% of these cases. The rate of secondary stent failure was 10.9%. All cases of secondary stent dysfunction were endoscopically managed. In patients who had received EUS-CDS in a neoadjuvant setting, only 1 patient could not complete the foreseen chemotherapy prior to Whipple surgery because of a procedure-related adverse event.

Conclusions: EUS-CDS is an effective and safe mode of biliary drainage in patients with distal biliary obstruction, both in a palliative and neoadjuvant setting. LAMS maldeployment was rare and took place in patients with a common bile duct diameter $\leq 12\text{mm}$. Presence of an upstream duodenal substenosis resulted in a high rate of primary stent dysfunction.

-G09-

OPTIMAL TIMING TO REDUCE INCOMPLETE VISUALISATION OF THE SMALL BOWEL USING WIRELESS CAPSULE ENDOSCOPY. T. Moreels (1) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Hepatogastroenterology.

Introduction: Wireless capsule endoscopy (WCE) is a first-line examination for suspected small bowel bleeding. Capsule retention due to mechanical stricture in the gastrointestinal (GI) tract is a known adverse event leading to incomplete WCE examination. Incomplete WCE can also be related to functional motility disorders of the GI tract or to insufficient recording time.

Aim: Assessment of optimal recording time to reduce incomplete WCE due to functional motility disorders.

Methods: Single-centre retrospective study of consecutive WCE examinations using different types of capsules: EndoCapsule S10, Pillcam SB3, OMOM and ANKON. Daytime (between 9h00 and 16h00) and overnight recordings were performed. All WCE were read in the conventional modus with a reading speed between 5 and 10 images/sec without the use of artificial intelligence.

Results: A total of 210 consecutive WCE examinations were analysed in 117 male ($69\pm 1\text{y}$) and 93 female ($65\pm 2\text{y}$) patients (age range 14-92y). Suspected small bowel bleeding was the leading indication (97%), except for $n=7$ patients. Bleeding presented as iron deficiency anaemia (66%), melena (26%) or unexplained rectal bleeding (8%) after normal upper and lower GI endoscopy. In 17% of all WCE active GI bleeding was diagnosed and in 41% potentially bleeding lesions like arteriovenous malformations, blue rubber bleb naevi, erosions or polypoid and tumoural lesions. In 29% the (potentially) bleeding lesions were located in the upper GI tract and in 6% in the lower GI tract within the reach of conventional endoscopy. In 34% WCE turned out to be normal. 37% of patients were referred for device-assisted enteroscopy based on the WCE findings. A total of 28 WCE (13%) were incomplete with the capsule not reaching the colon, with 7 because of technical failure ($n=2$) or mechanical stricture ($n=5$). The remaining 21 incomplete WCE were due to short recording time relative to the transit time (23% incomplete WCE when $<10\text{h}$ recording time vs 3% incomplete WCE when $<15\text{h}$ vs 1% incomplete WCE when $>15\text{h}$; $p=0.0012$ Chi-square).

Conclusions: WCE is an important first-line examination for suspected small bowel bleeding, with 17% of active bleeding recorded and an additional 41% of potentially bleeding lesions. However, those lesions are often found in the upper (29%) and in the lower (6%) GI tract despite prior normal upper and lower GI endoscopy. To avoid incomplete WCE due to slow GI transit a recording time of at least 15h seems mandatory.

-G10-

OBJECTIVE AND CONTINUOUS ASSESSMENT OF BOWEL PREPARATION QUALITY USING DEEP LEARNING-BASED SCENE SEGMENTATION. L. Jans (1), P. Sinonquel (2), T. Eelbode (3), O. Pech (4), D. De Wulf (5), P. Dewint (6), H. Neumann (7), G. Antonelli (8), F. Iacopini (8), D. Tate (9), A. Lemmers (10), N. Pilonis (11), M. Kamiński (11), H. Cesare (12), I. Demedts (2), P. Roelandt (2), R. Bisschops (2), F. Maes (1) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Electrical Engineering (ESAT/PSI), [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Translational Research in Gastrointestinal Disorders, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Electrical Engineering (ESAT/PSI), [4] Krankenhaus Barmherzige Bruder Regensburg, Regensburg, Germany, Gastroenterology and Hepatology, [5] AZ Delta, Belgium, Gastroenterology and Hepatology, [6] AZ Oostende, Oostende, Belgium, Gastroenterology and Hepatology, [7] Gastrozentrum Lippe, Bad Salzuflen, Germany, Gastroenterology and Hepatology, [8] Ospedale del Castelli, Rome, Italy, Gastroenterology and Digestive Endoscopy Unit, [9] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology and Hepatology, [10] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, HUB (Hôpital Universitaire de Bruxelles), [11] National Institute of Oncology, Warsaw, Warsaw, Poland, Department of Gastroenterological Oncology, [12] Humanitas University Hospital, Milan, Italy, Endoscopy.

Introduction: Bowel preparation quality is a key determinant of colonoscopy effectiveness, influencing mucosal assessment and lesion detection. The Boston Bowel Preparation Scale (BBPS) is a widely used scoring system, yet its categorical and subjective nature limits granularity and consistency. **Aim:** This study aims to develop and validate a deep learning model for automated, objective, and continuous assessment of bowel cleanliness using real-time image analysis.

Methods: A retrospective dataset of colonoscopy videos from nine international centres (n=1128; 2020–2022; white light imaging) was used to train a DeepLabV3+ model¹ for seven-class scene segmentation (stool, water, clean mucosa, instruments, borders, shadows, glare). For validation, the trained model was applied to an independent single-centre dataset of colonoscopy videos (n=428; 2023–2024; white light and narrow band imaging). The model processed these videos by extracting one frame per second and generating a segmentation output for each extracted frame. From these outputs, we derived AI cleanliness metrics: frame-wise fractions of stool, water, and clean mucosa, and a novel Normalised Stool Index (NSI), defined as the proportion of the total mucosa labelled as stool, which is less biased by artifacts than the stool fraction. All metrics were computed only from instrument-free withdrawal frames, matching BBPS scoring conventions, and averaged per procedure. Associations between total BBPS scores from two raters (R1, R2; quadratic weighted $\kappa=0.22$; inter-rater $\rho=0.221$; weak inter-rater reliability) and mean stool, water, and clean mucosal fractions, as well as NSI, were assessed (Spearman's ρ with false-discovery-rate correction). Clinical relevance was examined by correlating mean NSI, water fraction, and Δ NSI (difference between withdrawal and insertion) with lesion count and minimum lesion size, and by assessing the ability of the AI cleanliness metrics to predict the presence of at least one adenoma (AUC and logistic regression). Expected behaviour was assessed by examining NSI changes between scope insertion and withdrawal and around automatically detected rinsing events (paired Wilcoxon signed-rank test).

Results: The DeepLabV3+ model achieved strong segmentation performance (sensitivity 92.7%, specificity 98.1%, mean Dice 93.8%), enabling reliable extraction of the AI cleanliness metrics. Withdrawal NSI showed the strongest association with BBPS, with significant correlations for both raters (R1: $\rho=-0.21$; R2: $\rho=-0.12$; both $p<0.02$). Stool fraction showed a similar pattern (R1: $\rho=-0.19$; R2: $\rho=-0.12$; both $p<0.02$). Water fraction correlated positively with BBPS for R2 only ($\rho=0.17$; $p<0.001$), and clean mucosal fraction showed no significant association. Cleanliness metrics showed no significant correlations with lesion count or minimum lesion size (all $|\rho|<0.12$; $p>0.10$), and showed no discriminative ability for adenoma presence prediction (AUC ≈ 0.5). Logistic regression yielded non-significant odds ratios (OR) for all tested metrics (ORs 0.92–1.12; $p>0.2$). NSI decreased significantly after rinsing events (mean Δ NSI=-0.77%, $p<0.001$) and improved between insertion and withdrawal (mean Δ NSI=-1.59%, $p<0.05$).

Conclusions: The segmentation model performed strongly across all classes, enabling reliable extraction of the AI cleanliness metrics. NSI had the strongest association with BBPS, weaker trends were demonstrated for stool and water fractions. These modest correlations are expected given BBPS's limited inter-rater agreement and its selective, segment-based scoring, which does not account for the effects of rinsing. Clinical outcome analysis was constrained by the cohort's high adequacy rate (98%) and the use of procedure-level averages, which cannot reflect visibility at specific lesion sites. The AI cleanliness metrics behaved as expected, with NSI improving from insertion to withdrawal and decreasing in response to rinsing. Together, these findings show that the novel AI system provides a continuous and detailed quantification of bowel cleanliness, capturing real-time changes and offering scene context that may support automated reporting and enhance downstream tools such as polyp detection. Further work in procedures with greater variability in preparation quality is needed, but the present results establish a strong foundation for more objective, reproducible, and clinically meaningful cleanliness assessment.

¹ Liang-Chieh Chen, Yukun Zhu, George Papandreou, Florian Schroff, Hartwig Adam. Encoder-Decoder with Atrous Separable Convolution for Semantic Image Segmentation, Proceedings of the European Conference on Computer Vision (ECCV), 2018, pp. 801-818.

-G11-

ERGONOMY IN ENDOSCOPY: TIME TO THINK. L. Triki (1), N. Ramdani (2), B. Ramdani (2), L. Eddahri (3), B. Simeti Naume (3), W. Sita Kianzambi (3), M. Pirson (3), A. Lemmers (1), M. Arvanitakis (1) / [1] HUB Hôpital Erasme, Brussels, Belgium, Gastroenterology, [2] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Physiotherapy, [3] HUB Hôpital Erasme, Brussels, Belgium, Nurse Department of Endoscopy HUB Erasme Hospital.

Introduction: Musculoskeletal disorders (MSDs) are caused by repetitive and non-physiological constraints.

Aim: The primary objective of this study was to determine the prevalence and localization of MSDs among health care professionals (HCPs) in endoscopy units; the secondary objective was to identify risk factors.

Methods: Questionnaires were distributed in French-speaking hospitals in Belgium—one for physicians and one for nurses. It was distributed between February 2025 and the end of April 2025. It was circulated through the communication channels of the Belgian Royal Society of Gastroenterology (SRBGE) and within Gastroenterology departments both electronically via QR code and in paper format made available in the departments' staff break rooms. To also include the trainees, the questionnaires were distributed to the ULB network's Gastroenterology clinical supervisors. Collected data included demographics, occupational background, and self-reported MSDs. Correlation tests were performed to assess the association between potential risk factors (sex, hand size, physical and endoscopic activity) and the presence of MSDs.

Results: A total of 63 physicians and 42 nurses participated, representing a variety of work settings (university hospitals, private practices, retired professionals, and trainees). Among physicians, 84.1% reported at least one MSD. The most affected anatomical region was the thumb (55.6%), followed by the lower back (54%), and hands (42.9%). Among nurses, 97.6% reported MSDs, with the lumbar region most affected (85.7%), followed by the upper back (73.8%), and the neck and shoulder (69%). These symptoms affected work performance, leading to temporary work interruptions. In the physician group, 17.5% had taken sick leave due to MSDs, mainly attributed to lower-back pain (7.9%). In the nursing group, 54.8% reported temporary interruptions, again with the lumbar region being the most frequently involved (35.7%). Chi-square correlation tests were performed to evaluate the association between the occurrence of MSD and some risk factors but no statistically significant correlations were identified, probably due to the limited sample size.

Conclusions: This observational study reveals a high prevalence of MSDs among HCPs in endoscopy units, leading to a significant impact on work performance.

**BELGIAN SOCIETY FOR GASTROINTESTINAL ENDOSCOPY (BSGIE)
- FRIDAY VIDEO SESSION**

-GV01-

ENDOSCOPIC SUBMUCOSAL DISSECTION OF A GASTRIC GIST USING A RIGIDIZING OVERTUBE TO FACILITATE STABILIZATION IN A DIFFICULT UPPER STOMACH LOCATION. M. Michelon (1), L. Verset (2), S. Ouazzani (1), S. Teles de Campos (1), P. Eisendrath (3), A. Lemmers (1) / [1] Hôpital Erasme, ULB, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, [2] Hôpital Erasme, ULB, Belgium, Department of Pathology, [3] CHU Saint-Pierre, Brussels, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology.

Endoscopic submucosal dissection (ESD) of subepithelial lesions (SELs) is challenging in the upper gastric body and fundus, where unstable scope positioning and limited visualization hinder dissection. These factors increase the risk of incomplete resection or perforation, especially during dissection of lesions from the muscularis propria. A strategy to improve scope stability in this region is needed. We report stabilization-assisted ESD using a rigidizing overtube to achieve en bloc resection of a gastric GIST from the muscularis propria, in its first reported use in upper gastrointestinal ESD. The overtube, which becomes rigid through vacuum activation, stabilized the endoscope shaft and maintained a fixed trajectory despite anatomy and a gravity-dependent lesion near the cardia. This improved control, reduced unintended movements, and allowed access to deeper components of the lesion. After submucosal injection, a circumferential incision was performed with an ESD knife, followed by excavation-type dissection using a hook-type knife under clip-line traction. The lesion was separated from the muscularis propria without perforation and removed en bloc in 150 minutes. The defect was closed with clips. The specimen measured 35 × 30 mm with intact capsule. Histology confirmed R0 resection of a 29 mm GIST with low mitotic activity. The postoperative course was uneventful, with discharge the next day. Endoscopic and radiologic surveillance was proposed. This represents the first reported use of a rigidizing overtube for ESD in the upper gastrointestinal tract and demonstrates its value in improving stability and enabling resection of gastric SELs in challenging regions.

-GV02-

ENDOSCOPIC SUBMUCOSAL DISSECTION OF A RARE SOLITARY EXTRAMEDULLARY PLASMACYTOMA OF THE GASTRIC CARDIA. M. Michelon (1), S. Ouazzani (1), L. Verset (2), A. Lemmers (1) / [1] Hôpital Erasme, ULB, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, [2] Hôpital Erasme, ULB, Belgium, Department of Pathology.

Gastric solitary extramedullary plasmacytoma is a rare entity, accounting for less than 5% of all extramedullary plasmacytomas. Endoscopic and radiologic appearance often mimics subepithelial tumours such as GIST or leiomyoma, making diagnosis challenging. We report a case of a solitary gastric cardia plasmacytoma successfully treated by endoscopic submucosal dissection (ESD). A 74-year-old woman with a history of monoclonal gammopathy of undetermined significance (MGUS) underwent evaluation after incidental detection of focal radiotracer uptake on vascular scintigraphy. Upper endoscopy revealed a subepithelial lesion at the gastric cardia, with initial biopsies and two endoscopic ultrasound (EUS)-guided sampling attempts remaining non-diagnostic. Positron Emission Tomography/Computed Tomography (PET/CT) showed a markedly hypermetabolic lesion (SUVmax ~16) without regional or distant involvement. A third EUS showed a 12 mm hypoechoic lesion arising from the muscularis propria. Cytology demonstrated plasmacytoid cells expressing CD138, MUM1 and kappa light chain restriction, confirming plasmacytoma. Staging with Magnetic Resonance Imaging (MRI), PET/CT, bone marrow biopsy, serum electrophoresis and free light chain assay revealed no systemic involvement. Curative resection by ESD was performed, achieving en-bloc removal of a 20 mm lesion (specimen 45 × 35 mm) without complications. Histopathology confirmed a kappa-restricted plasmacytoma with negative margins (R0 resection). At 7 months, PET/CT demonstrated complete resolution of hypermetabolic activity, and surveillance endoscopy showed a well-healed ESD scar without recurrence. This case highlights the role of EUS, cytology with immunohistochemistry, and advanced endoscopic resection in diagnosing and managing rare gastric plasmacytomas. ESD represents an effective curative approach for selected localized lesions.

BELGIAN INFLAMMATORY BOWEL DISEASE RESEARCH AND DEVELOPMENT GROUP (BIRD)

-I01-

APICAL-OUT ORGANOID DERIVED FROM UC PATIENTS AS A MODEL TO INVESTIGATE EPITHELIAL ER STRESS-INDUCED FIBROSIS INDEPENDENT OF INFLAMMATION. M. Stepniak (1), A. Pierre (1), C. Salée (1), C. Massot (1), S. Vieujean (2), C. Reenaers (2), J. Loly (2), S. Specca (3), C. Coimbra (4), E. Decker (4), P. Delvenne (5), N. Blétard (5), S. Beq (6), E. Louis (2), M. Meuwis (1) / [1] GIGA Institute, University of Liège, Liège, Belgium, Translational Gastroenterology, [2] CHU de Liège, Liège, Belgium, Hepato-gastroenterology and digestive oncology, CHU of Liège, BE, [3] University of Lille, Inserm, CHU Lille, France, Faculté de Médecine, Pôle Recherche - LIRIC - UMR 995, [4] CHU de Liège, Liège, Belgium, Abdominal surgery CHU of Liège, BE, [5] CHU de Liège, Liège, Belgium, Pathological anatomy, CHU of Liège, BE, [6] Thabor Therapeutics, France, R&D.

Introduction: Ulcerative colitis (UC) is an Inflammatory bowel disease (IBD) with diffuse colonic mucosal inflammation. Fibrosis which has been observed in the submucosa and muscularis mucosae even without active inflammation¹, remains underexplored in UC. No anti-fibrotic treatment has been proven clinically efficient to cure fibrosis in IBD. At the epithelial level, IBD-related endoplasmic reticulum stress (ERS) and inflammation upregulate ER chaperones like AGR2, which, when secreted (eAGR2), can induce fibroblast-to-myofibroblast transition (FMT) suggesting a role for eAGR2 and ERS in fibrosis². Beside eAGR2 other factor might be released by stressed epithelium and drive fibrosis progression. **Aim:** Our aim is to better understand the role played by the epithelium in UC intestinal fibrosis initiation and progression. We are using a pro-fibrotic organoid apical-out³ model derived from UC patients challenged by transient ERS⁴ induction without inflammation drivers.

Methods: On organoids derived from 12 UC patients, we induced transient ERS using Tunicamycin (Tm), followed by a recovery period in fresh culture medium, allowing observations of the epithelial post-stress response. RNA, protein extracts and culture supernatants were analysed to assess ERS markers, epithelial-mesenchymal transition (EMT), pro-fibrotic factors (TGF- β 1, eAGR2). Organoids were also evaluated by immunofluorescence (IF) targeting AGR2 and sXBP1. Pre-conditioned culture supernatants were used in a functional assay where intestinal fibroblasts (CCD18-Co) were exposed to preconditioned supernatant to assess FMT (IF α -SMA increase). We also performed an ELISA dosage of the active eAGR2 fraction in recovery supernatants. Bulk RNAseq transcriptomic analysis was done to confirm the biomolecular patterns and investigate the molecular changes characterizing this epithelial profibrotic phenotype.

Results: After 12 hours of transient Tm stimulation and 32-hour recovery, all Apical out organoids showed a statistically significant increased expression of the ERS markers (BIP/CHOP/sXBP1) by RT-qPCR. The fold changes Tm/CTL ranged from 6 to 20, 4 to 28, and 3 to 8 respectively. AGR2 was significant more elevated in stimulated compared to control conditions, with a median relative fold change of 7.57 (range: 2,33 to 15,89). No pro-inflammatory cytokine nor TGF- β 1 were statistically increased during the recovery period. In WB, eAGR2 was detected in all culture supernatants and increased under Tm compared to vehicle with absence of cellular lysis (except for one patients). BIP was detected only after Tm stimulation. Active eAGR2 ELISA levels in supernatants were statistically increased post-ERS (Tm/CTL eAGR2 median fold change: 1.77, Range (min et max). α -SMA signal increased in CCD-18 Fibroblasts attesting of FMT (44 to 120% more intense in Tm cdts /vehicle). RNAseq data confirmed the ERS increased activation as UPR using Dseq2 differential analysis and using GSEA.

Conclusions: We studied the ERS-induced epithelial responses of organoids derived from UC patients and showed their pro-fibrogenic effect on FMT, independently of pro-inflammatory drivers. This suggests that epithelial secretome ERS response is able to promote FMT, a hallmark of intestinal fibrosis. The specific role of eAGR2 and other molecular changes characterising this organoid induced phenotype is under further investigation by multi-Omics including paracrine factors.

-I02-

ENDURING NEUROINFLAMMATION IN THE PREFRONTAL CORTEX FOLLOWING CHRONIC COLITIS: A ROLE FOR C1Q? H. Lernout (1), M. Truyens (2), C. De Nolf (3), C. Vandendriessche (3), A. Bruggeman (4), J. Xie (5), S. Van Welden (6), T. Lobatón (2), M. De Vos (2), V. Vermeirssen (7), S. Van Welden (6), R. Vandenbroucke (3), D. Laukens (6) / [1] Universiteit Gent, Gent, Belgium, Internal Medicine and Paediatrics, [2] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology, [3] Ghent University,

Ghent, Belgium, VIB Centre for Inflammation Research, [4] University Hospital Ghent (UZ Gent), Gent, Belgium, Neurology, [5] Nanchang University, Jianxi, China, State Key Laboratory of Food Sciences and Resources, [6] Ghent University, Ghent, Belgium, Internal Medicine and Paediatrics, [7] Ghent University, Ghent, Belgium, Biomolecular Medicine.

Introduction: Fatigue is an impactful psychological comorbidity among patients with inflammatory bowel disease (IBD) that often persists during disease remission. Interestingly, we previously demonstrated that mice also exhibit fatigue-like behaviour post-colitis, which coincides with persistent neuroinflammation (Truyens et al., *Journal of Crohn's and Colitis* (2023)). Complement component 1q (C1q) was identified as a hub mediator underlying the inflammatory signature.

Aim: The aim of this study was to uncover a mechanistic link explaining this persistent neuroinflammation, and to translate these findings to fatigue in patients with IBD in remission.

Methods: Extinguished chronic colitis (cDSS) was induced in female C57BL/6J mice by cyclic administration of 2% dextran sodium sulphate, followed by a four-week recovery period. C1q serum levels were measured using ELISA, and neuroinflammation was assessed by qPCR. A blood-cerebrospinal fluid barrier was set up in vitro using human choroid plexus endothelial cells (iHCPEnC) and choroid plexus epithelial cells (HIBCPP) grown on the inside and outside, respectively, of a Transwell® filter membrane, and placed over human microglia cells (HMC3). C1q (250 µg/mL) was added to the endothelial side of the filter insert. Barrier strength was measured via transepithelial electrical resistance (TEER), and HMC3 activation was assessed by qPCR. The serum C1q concentration of patients with IBD in remission included in a previous clinical trial (Truyens et al., *Gastroenterology* (2022)) was measured using ELISA.

Results: Serum C1q levels were numerically higher in cDSS mice compared to controls ($P=0.059$, control: $135.5\mu\text{g/mL}\pm 57.2$, cDSS: $191.9\mu\text{g/mL}\pm 58.7$) and correlated positively with the expression of Lcn2 ($r=0.50$, $P=0.03$), S100a8 ($r=0.56$, $P=0.01$), and S100a9 ($r=0.51$, $P=0.02$) in the prefrontal cortex. The administration of C1q to the endothelial side of the in vitro choroid plexus model induced a drop in the TEER after 24h ($P=0.009$, control: $110.8\%\pm 12.6$, 250 µg/mL C1q: $69.5\%\pm 11.3$), indicating compromised barrier integrity. Moreover, the relative gene expression of microglia activation markers TNFα ($P=0.035$, control: $1\text{NRQ}\pm 0.74$, C1q administration: $2.59\text{NRQ}\pm 0.47$), P2RY12 ($P=0.056$, control: $1\text{NRQ}\pm 0.65$, C1q administration: $0.23\text{NRQ}\pm 0.084$), and CD68 ($P=0.012$, control: $1\text{NRQ}\pm 0.082$, C1q administration: $0.75\text{NRQ}\pm 0.089$) was disturbed. In a retrospective analysis of patients with quiescent IBD, serum C1q levels correlated significantly with fatigue severity, as measured by the fatigue visual analogue scale (fVAS) ($r=0.24$, $P=0.01$).

Conclusions: We demonstrated that C1q may play a key role in the persistence of neuroinflammation during asymptomatic chronic colitis and could represent a promising therapeutic target for alleviating fatigue in IBD patients.

-I03-

DEVELOPMENT OF A HUMAN MULTI-ORGAN-ON-CHIP MODEL TO UNRAVEL GUT-BRAIN COMMUNICATION IN THE CONTEXT OF IBD. L. Maes (1), Y. Waegemans-Rosiers (1), S. Van Welden (2), R. Vandenbroucke (3), D. Laukens (1) / [1] Ghent University, Ghent, Belgium, Department of Internal Medicine and Paediatrics, [2] Ghent University, Ghent, Belgium, Department of Bioanalysis, [3] VIB-UGent Centre for Inflammation Research, Gent, Belgium, Department of Biomedical Molecular Biology.

Introduction: Persistent fatigue severely affects the quality of life of inflammatory bowel disease (IBD) patients and reduces their ability to work. Although IBD patients, even in clinical remission, report fatigue as one of the most disabling symptoms of their chronic disease, disease management is often only focused on attenuating gastrointestinal symptoms. In order to develop effective therapeutic interventions, a better understanding of gut-brain communication causing IBD-associated fatigue is required.

Aim: The goal of this project was to establish a human in vitro multi-organ-on-chip model to explore the impact of extinguished gut inflammation on brain and brain barrier function.

Methods: In our model, a gut-blood barrier, comprising of Caco-2 (enterocytes) and HT29-MTX cells (goblet cells), was connected to a blood-cerebrospinal fluid (CSF) barrier, composed of HIBCPP and iHCPEnC cells (choroid plexus epithelial and endothelial cells respectively), and to a brain compartment (SH-SY5Y, neurons) via recirculation of cell culture medium. Gut inflammation was mimicked by the addition of the 25 ng/mL TNFα and 25 ng/mL IFNγ to the intestinal epithelial cells. Barrier integrity was measured by transepithelial/endothelial electrical resistance (TEER) and by paracellular permeability assays with 4 kDa FITC-dextran. In addition, we performed a bead-based immunoassay to measure secreted IL-8 levels and analysed differential gene expression levels via RNA sequencing and RT-qPCR.

Results: Under low perfusion (9.1×10^{-4} mPa), the gut–blood barrier showed increased expression of differentiation marker genes compared with static culture, including LYZ ($p < 0.01$), ALPI ($p < 0.01$), and CYP3A4 ($p < 0.001$), indicating enhanced cellular differentiation. Low perfusion also promoted the formation of 3D villus-like structures, mucus production, and a shift in barrier integrity toward physiologically relevant levels (TEER: $81.6 \pm 44.8 \Omega \cdot \text{cm}^2$; Papp: $1.1 \times 10^{-6} \pm 1.2 \times 10^{-6}$ cm/s). The blood-CSF barrier under low perfusion (endothelial: 22 mPa; epithelial: 1.2×10^{-3} mPa) formed a tight and functional barrier (TEER: $852.3 \pm 60.4 \Omega \cdot \text{cm}^2$; Papp: $1.1 \times 10^{-7} \pm 5.5 \times 10^{-8}$ cm/s). Neurons differentiated using BDNF and retinoic acid developed long dendrites and showed increased expression of mature neuronal marker genes (SYP ($p < 0.001$), SNAP25 ($p < 0.001$), TUBB3 ($p < 0.001$), ACHE ($p < 0.001$)) compared with undifferentiated cells. The gut-blood barrier responded to TNF α and IFN γ stimulation with elevated IL-8 secretion in the circulating blood medium (219.0 ± 98.3 pg/mL; $p < 0.05$). After 24 h of interaction with the blood-CSF barrier and brain compartment, IL-8 levels returned to baseline (102.5 ± 36.6 pg/mL), indicating resolution of gut inflammation. RNA sequencing at the blood-CSF barrier, followed by gene set enrichment analysis, revealed upregulation of genes associated with the GO terms ‘response to cytokine’, ‘cytokine production’, and ‘regulation of cytokine production’.

Conclusions: This project established a physiologically relevant human multi-organ-on-chip model integrating gut, blood-CSF barrier, and neuronal compartments that respond to a pro-inflammatory trigger. The platform enables the mechanistic investigation of how extinguished gut inflammation affects brain and brain barrier function. As a next step, we will integrate patient-derived material to clarify how brain and brain barrier alterations contribute to fatigue.

-104-

A PREDICTIVE AND DRUGGABLE BIOMARKER FOR POSTOPERATIVE RECURRENCE IN CROHN’S DISEASE: INTESTINAL EPITHELIAL GPX4. S. Verstockt (1), J. Schwärzler (2), P. Willeit (3), G. Bislenghi (4), M. Meyer (2), L. Mayr (2), K. Machiels (5), G. De Hertogh (6), M. Lenfant (1), L. Scheffauer (2), F. Grabherr (7), D. Jans (8), S. Abdurahiman (1), I. Cleynen (8), A. Jukic (2), L. Zundel (2), P. Moser (9), L. Forer (10), M. Witsch-Baumgartner (11), M. Ferrante (12), J. Sabino (12), A. D’Hoore (4), M. Hess (13), A. Kaser (14), R. Blumberg (15), R. Koch (2), L. Le Bourhis (16), N. Hammoudi (16), D. Cazals-Hatem (17), S. Vermeire (1), H. Tilg (2), M. Allez (16), T. Adolph (2), B. Verstockt (12) / [1] Translational Research Centre for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism, [2] Medical University of Innsbruck, Innsbruck, Austria, Department of Internal Medicine I, [3] Medical University of Innsbruck, Innsbruck, Austria, Institute of Clinical Epidemiology, Public Health, Health Economics, Medical Statistics and Informatics, [4] University Hospitals Leuven (UZ Leuven), Leuven, Belgium, Department of Abdominal Surgery, [5] Pfizer, Elsenne, Belgium, [6] University Hospitals Leuven (UZ Leuven), Leuven, Belgium, Department of Pathology, [7] Medical University of Innsbruck, Innsbruck, Austria, Department of Chronic Diseases and Metabolism, [8] KU Leuven, Leuven, Belgium, Department of Human Genetics, [9] Medical University of Innsbruck, Innsbruck, Austria, INNPATh, [10] Medical University of Innsbruck, Innsbruck, Austria, Institute of Genetic Epidemiology, [11] Medical University of Innsbruck, Innsbruck, Austria, Institute of Human Genetics, [12] University Hospitals Leuven (UZ Leuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [13] Medical University of Innsbruck, Innsbruck, Austria, Institute of Histology & Embryology, [14] Cambridge University, Cambridge, United Kingdom, Division of Gastroenterology and Hepatology, Department of Medicine, [15] Harvard Medical School, Boston, United States, Gastroenterology Division, Department of Medicine, [16] Beaujon Hospital, APHP, Paris Cité University, France, INSERM U1342, Institut de Recherche Saint-Louis, [17] Beaujon Hospital, APHP, Paris Cité University, France, Department of Pathology.

Introduction: Postoperative recurrence in Crohn’s disease (CD) remains common, highlighting the need for biomarkers that optimize risk stratification and inform new therapeutic strategies. We previously discovered that intestinal epithelial Glutathione peroxidase 4 (GPX4), an antioxidative selenoprotein that protects against ileitis, is reduced in postoperative endoscopic recurrence (ePOR).

Aim: Here, we evaluate intestinal epithelial GPX4 at the time of resection as a predictive biomarker for ePOR, and investigate therapeutic strategies to boost its function in the ileum.

Methods: To assess the predictive value of GPX4, three independent, European ileocolonic resection (ICR) cohorts were included ($n = 241$ CD patients), with availability of ileocolonic resection specimens. Intestinal epithelial GPX4 protein expression was quantified on FFPE ileal tissue sections using quantitative confocal microscopy. ePOR was defined as Rutgeerts score $\geq$ i2b at ~ 6 months after ICR, and compared to complete absence of endoscopic activity (i0). Mechanistic pathways, including endoplasmic reticulum (ER) stress, were

examined using RNA sequencing of post-ICR ileum (n=36). To investigate functional relevance, three murine enteritis models were evaluated with (i) Gpx4 loss in intestinal epithelial cells (IECs) (Gpx4-/-IECΔERT2); (ii) epithelial ER stress (X-box-binding protein 1; Xbp1-/-IEC); and (iii) their combined state (i.e. Xbp1-/-IEC/Gpx4+/-IEC). Therapeutic rescue was tested using oral selenium. Statistical analyses were performed with Graph Prism 10.0, SPSS v. 21, MacQIIME v1.9.1 and R 4.3.2.

Results: Included patients across the three European ICR cohorts had a mean (±SD) age of 36 (±13) years, 52% were female, 41% had penetrating disease, and 35% were current smokers. Reduced intestinal epithelial GPX4 expression predicted ePOR in a patient-level meta-analysis across these cohorts. In particular, lower GPX4 expression was inversely and approximately log-linearly associated with higher odds of ePOR. Each 1-SD decrease in GPX4 expression significantly increased ePOR risk, also after multivariable adjustment (OR 1.78, 95%CI 1.22–2.58; P<0.001). Importantly, GPX4 expression was unrelated to GPX4 genetic variation (rs2024092, P=0.60), histologic severity of inflammation (Geboes Grade, P=0.792), or established clinical risk factors (sex: P=0.370, penetrating disease: P=0.646, or active smoking (P=0.532)). Adding GPX4 to a model with established clinical risk factors significantly improved the prediction of ePOR (AUROC from 0.638 to 0.707; P=0.014). Mechanistically, reduced GPX4 correlated with ER stress signatures (r= -0.77; P=3.0×10⁻⁸). In mice, epithelial ER stress combined with reduced GPX4 triggered severe spontaneous enteritis (Xbp1-/-IEC/Gpx4+/-IEC mice) (P<0.01), indicating that GPX4 normally compensates for ER-stress-driven enteritis. Reinforcing this GPX4 buffer proved therapeutic: oral selenium boosted epithelial GPX4 and ameliorated enteritis in Xbp1-/-IEC mice—an ER-stress model with reduced GPX4 (P<0.05)—but did not in inducible Gpx4-deficient mice (Gpx4-/-IECΔERT2) (P>0.05). This demonstrates that the anti-inflammatory effect of selenium depends on intestinal epithelial GPX4 function.

Conclusions: This study identifies intestinal epithelial GPX4 as a druggable biomarker that improves the prediction of ePOR in CD, potentially guiding patient-tailored management of CD after ileocolonic resection.

-I05-

DISTINCT EPITHELIAL REMODELLING PROGRAMS UNDERPIN SURGICAL REPAIR FEASIBILITY AND HAVE POTENTIAL TO REFINE CLINICAL ASSESSMENT. S. Abdurahiman (1), J. Sabino (1), S. Verstockt (1), K. Johnson (1), L. Giorio (1), K. Arnauts (1), C. Caenepeel (1), M. Lenfant (1), M. Ferrante (1), J. Raes (2), A. D’Hoore (3), S. Vermeire (1), G. Bislenghi (3), B. Verstockt (1) / [1] KU Leuven, Leuven, Belgium, Translational Research in Gastrointestinal disorders TARGID- Department of Chronic Diseases and Metabolism CHROMETA, Leuven, Belgium., [2] Rega Institute- KU Leuven, Leuven, Belgium, Laboratory of Molecular Bacteriology, Department of Microbiology and Immunology, Rega Institute, KU Leuven, Leuven, Belgium, [3] University Hospitals Leuven (UZ Leuven), Leuven, Belgium, Department of Abdominal Surgery, Colorectal Surgery, UZ Leuven, KU Leuven, Leuven, Belgium.

Introduction: Perianal fistulising Crohn’s disease (pCD) affects 20-50% of Crohn’s disease (CD) patients with ~90% requiring a surgical procedure at least once. The recently proposed TopClass framework provides a pragmatic clinical classification of pCD1. Class 2a denotes patients suitable for repair through medical-surgical management, whereas classes 2b or higher denotes stages where symptom control rather than repair becomes the primary treatment goal. However, the molecular mechanisms underlying these clinical subtypes remain poorly defined.

Aim: To delineate the molecular architecture of perianal fistulising Crohn’s disease by performing transcriptomic profiling of paired rectal and fistula tissues, and to uncover inter-patient heterogeneity through integrated multi-dimensional analysis.

Methods: Paired biopsies from two sites - the fistula tract and rectal orifice of 54 unique patients (n=44 CD, n=10 Cryptoglandular fistula (CPTGL)), supplemented by longitudinal samples to have a total of 81 profiles (70 CD and 11 CPTGL) - underwent bulk RNA sequencing to generate site paired transcriptomic datasets. Multi-Omics Factor Analysis (MOFA) was applied, followed by hierarchical clustering and weighed gene co-expression network analysis (WGCNA) to characterise patient subgroups.

Results: Integration and unsupervised clustering of paired fistula and rectal transcriptomes identified three molecular patient subgroups (C1, C2, C3), independent of concomitant proctitis or diagnosis (p>0.05). Molecular characterization of the gene programs revealed distinct epithelial remodelling patterns specific to each patient subgroup. C1 and C2 were both driven by epithelial-mesenchymal transition (EMT) in the fistula but differed in their rectal programs. However, C3 showed a uniquely different molecular profile in the fistula with strong keratinization signature instead of EMT. In the rectum, C1 and most of C3 displayed homeostatic glycosylation patterns while C2 exhibited keratinization in the rectum similar to C3 fistula.

Notably, C3 patients were significantly enriched for TopClass 2a, indicating suitability for surgical repair ($p<0.05$). Among patients with recent MR imaging available ($n = 10$: 2a; $n = 13$: 2b), we observed that the C2 subgroup exhibited higher MAGNIFI-CD2 inflammatory mass sub-score ($p<0.05$), suggesting a more aggressive disease phenotype. Consistent with this, of all the TopClass 2a patients, those belonging to C2 molecular subgroup had a significantly increased risk of requiring ileostomy ($p<0.05$).

Conclusions: This study demonstrates a clinically meaningful molecular stratification of pCD by assigning distinct epithelial remodelling signatures—independent of proctitis—to three patient classes. These classes exhibit clear clinical distinctions, separating repair-amenable presentations from more aggressive disease associated with higher inflammatory burden and progression to ileostomy within TopClass 2a.

-I06-

INDEPENDENT EFFECTS OF MEDITERRANEAN DIET AND DONOR-DEPENDENT FMT ON DISEASE ACTIVITY AND GUT MICROBIOTA IN A HUMANIZED UC MODEL. S. Deleu (1), S. Troisi (2), L. Masi (2), K. Vidmar (3), V. Emoli (2), C. Pane (2), G. Migliore (2), E. Foscari (2), F. Profeta (2), H. Wargo (3), J. Williams (3), S. Artone (3), S. De Santis (3), C. De Salvo (3), F. Del Chierco (4), M. Scanu (4), L. Putignani (4), A. Papa (2), V. Petito (2), L. Lopetuso (2), F. Cominelli (3), T. Pizarro (3), F. Scaldaferri (2) / [1] Translational Research Centre for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Department of chronic diseases and metabolism, [2] Fondazione Policlinico Universitario, A. Gemelli, IRCCS, Rome, Italy, Rome, Italy, CeMAD Translational Research Laboratories, Digestive Disease Centre (CeMAD), Department of Medical and Surgical Sciences, [3] Case Western Reserve University, Cleveland, United States, Pathology, [4] Bambino Gesù Children's Hospital IRCCS, Rome, Italy, Unit of Microbiology.

Introduction: Faecal microbiota transplantation (FMT) has been shown to be a promising approach to treat active ulcerative colitis (UC), and donor effects have been observed^{1,2}. Both single- and multidonor FMTs have been used, but with ambiguous results. Also, diet plays a crucial role in shaping the gut microbiome and might affect the efficacy of FMT.

Aim: Therefore, we aimed to investigate the role of diet and different single-donor and their mixture as multidonor formulations in FMT efficacy exploiting a humanized IBD model.

Methods: Female C57BL/6 mice (8-11w) were treated with broad-spectrum antibiotics followed by humanization with either UC single-donor patient-derived microbiota, and subsequently randomized to either Western, Mediterranean or Control diet in combination with three distinct healthy single-donor FMT, a combination of these donors in a multidonor FMT or sham ($n=4$ /experimental grp). After one week, mice were subjected to DSS to induce acute colitis (7d, 2.5%), followed by another 7d of recovery. Disease activity indices (DAI) were determined and evaluated by area under the curve (AUC). Faeces were collected for 16S sequencing on day 6, 16 and 30. At sacrifice, blood and different tissues collected for histology, and RNA sequencing.

Results: Differences in disease activity can be observed and are initiated after introduction of DSS on day 16. Independent from FMT, Mediterranean diet was shown to improve disease, whereas a Western diet worsened disease outcomes (both $p<0.05$). Independently from diet, FMT seemed to improve disease and to be donor-dependent. The effect of FMT donor on DAI was not significantly influenced by dietary background (ANOVA, $p=0.65$). Donor 1 consistently showed the best outcomes across all diets, whereas donors 2, 3, and the multi-donor approach exhibited variable results that depended on the specific dietary background. Antibiotic treatment significantly reduced alpha diversity ($p<0.01$), which was restored after humanization and dietary introduction. After DSS treatment and recovery (day 30), animals on a Mediterranean diet had significantly higher alpha diversity given by observed richness ($p < 0.01$) compared to those on control and Western diets as well as compared to those not receiving DSS (healthy controls). Nevertheless, no differences were observed in terms of FMT origin ($p=0.91$). Histology and RNA sequencing results are in process.

Conclusions: Both Mediterranean diet and FMT independently reduced disease activity in a humanized UC mouse model, with FMT effects being donor-dependent and Mediterranean diet strongly increasing alpha diversity. No significant interaction between diet and FMT was observed, highlighting the need for further mechanistic studies.

-I07-

ESTABLISHING CORE REQUIREMENTS FOR IBD CLINICAL RESEARCH UNITS : A BELGIAN CONSENSUS AND PRACTICAL MODEL BASED ON PATIENT AND PROFESSIONAL INPUT. I. Arijis (1), L. Govaerts (2), L. Debrun (3), L. Fierens (4), K. Franc (5), H. Kelchtermans (6), C. Minsart (7), C.

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Introduction: Clinical research is essential to advance inflammatory bowel disease (IBD) care, yet no widely accepted framework currently defines the requirements of IBD clinical research units.

Aim: This study aimed to identify key components of an optimal IBD clinical research unit by integrating insights from healthcare professionals (HCPs) and patients, and to develop a practical model tailored to the Belgian setting.

Methods: A modified Delphi consensus process was conducted within the Belgian IBD Research and Development (BIRD) network, including two scoring rounds and a consensus meeting. Statements were rated on a 9-point scale. Those with $\geq 80\%$ agreement in the “essential” (scores 7-9) or “important but not essential” (scores 4-6) categories, or endorsed via consensus discussion, were incorporated into the final model.

Results: Consensus was achieved on 25 “essential” and 19 “important but not essential” statements for established research units, which were integrated into a practical toolbox structured across three frameworks: administrative, operational, and collaborative. The toolbox defines key components such as multidisciplinary team composition, sustainable financing through clinical studies, appropriate infrastructure, institutional support (clinical study, legal, and ethics departments), standardized procedures, feasibility assessments, team training and meetings, physician accessibility at study visits, and collaborations with hospital departments and external research networks. It also provides practical guidance for newly established units initiating IBD clinical research.

Conclusions: A structured model was developed to guide the establishment and optimization of IBD clinical research units, with potential applicability beyond Belgium and IBD.

-I08-

REAL-WORLD OUTCOME OF TEDUGLUTIDE IN ADULT PATIENTS WITH SHORT BOWEL SYNDROME AND INTESTINAL FAILURE IN BELGIUM: REDUCTION IN HOME PARENTERAL NUTRITION AND IMPROVEMENT IN PATIENT-PERCEIVED HEALTH STATUS. S. Vrancken (1), M. Arvanitakis (2), K. Geboers (3), L. Timmermans (3), N. Lauwers (3), A. Ballarin (2), H. De Schepper (4), A. Hadefti (2), A. Verbiest (1), L. Wauters (3), T. Vanuytsel (3) / [1] Translational Research Centre for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Leuven Intestinal Failure and Transplantation Centre (LIFT), [2] CUB Hôpital Erasme, Belgium, Department of Gastroenterology, [3] University Hospitals Leuven (UZ Leuven), Leuven, Belgium, Leuven Intestinal Failure and Transplantation Centre (LIFT), [4] Antwerp University Hospital, Edegem, Belgium, Department of Gastroenterology.

Introduction: Short bowel syndrome (SBS) is the main pathophysiological mechanism of chronic intestinal failure (IF), defined as a small bowel length $<200\text{cm}$, without (type 1) or with (type 2/3) colon-in-continuity. Patients with SBS-IF need home parenteral nutrition (HPN) for survival and maintaining homeostasis. Daily injections with teduglutide, a GLP-2 analogue which enhances spontaneous adaptation, significantly reduces HPN volume. Since June 2021, it has become available for patients with SBS-IF in Belgium.

Aim: To analyse the real-world effect of teduglutide on weekly HPN volume, patient-perceived health, and safety in the adult Belgian SBS-IF population.

Methods: In 2021 we started a prospectively maintained registry including all adult patients who were prescribed teduglutide in Belgium after signing the informed consent (Ethics Committee approval: S65901). Demographics, SBS- and HPN-related data, and patient global impression of change (PGIC) questionnaire were collected in REDCap at baseline (T0), three (T3), six (T6), and twelve (T12) months. There were no specific exclusion criteria other than contraindications for teduglutide. Teduglutide responders were defined as patients with a $\geq 20\%$ weekly HPN volume reduction in type 1 anatomy at T6. In type 2 and 3 anatomy, a responder was defined as a patient with a $\geq 20\%$ weekly HPN volume reduction with ≥ 1 day and ≥ 1 liter

reduction at T12, in accordance with the Belgian reimbursement criteria. All data entered before November 2025 were included. Descriptive statistics were used to summarize patient characteristics. The effect of teduglutide was measured using Wilcoxon paired signed rank tests with p-value significance set at 0.05. Data are shown as mean $\pm$ standard deviation or median (interquartile range) depending on the distribution.

Results: Twenty adult patients were included in the registry (70% female, n=14). Crohn's disease and intestinal ischemia were equally represented (n=8). The other patients had Hirschsprung's disease, trauma, cancer surgery or internal herniation as the underlying cause (all n=1). Age at start of teduglutide was 56.70 $\pm$ 13.69 years, and the duration of HPN before the start was 34 (24-85) months. Eight patients had SBS type 1, with a remaining bowel length of 112.50 $\pm$ 77.17 cm. Twelve patients were classified as type 2 (n=9) or 3 (n=3), with a bowel length of 73.10 $\pm$ 42.91 cm and 67.20 $\pm$ 28.20 % of colon-in-continuity. Five out of eight patients (62.5%) with type 1 anatomy were responders. Three non-responder patients stopped the treatment due to decreased appetite at T3 (n=1), deterioration of kidney function at T6 (n=1), and no effect at T12 (n=1). All eight patients with colon-in-continuity (type 2/3) who were treated for a year (T12) were responders (100%). Three patients did not yet reach T12 and one patient died at T6 due to recurrent mesenteric ischemia. The HPN volume was 6.50L (3.38-12.24L) at baseline, decreasing to 5L (2-9L, n=19, p<0.001 vs. baseline) at T3, remaining stable at T6 at 5L (2-7.41L, n=19, p<0.001) with further reduction at T12 to 3.97L (0-7L, n=14, p=0.002). Four patients (33%) with colon-in-continuity completely weaned off HPN before T12. Patient's weight also significantly increased from 62.30 $\pm$ 10.53kg at baseline to 64.22 $\pm$ 10.51kg at T12 (p=0.04, n=14). Teduglutide improved the perceived health status by the patient. At T3, 11/16 patients (68.75%) indicated "much" (n=6) or "very much" (n=5) improved health, and no worsening was reported. At twelve months, results were similar with 8/13 patients (61.54%) indicated a "much" (n=5) or "very much" (n=3) improved health. One patient reported a "very much worse" health status at T12 and dropped out afterwards because of no effect of the treatment. Eighty-four adverse events were reported in 19 patients. Sixty-nine were related to teduglutide: injection site reaction (n=15), change in stoma appearance (n=6), abdominal pain (n=20), nausea (n=16), vomiting (n=8), and hospitalization due to (sub)obstruction (n=2) and biliary problems (n=2). One patient decreased the dose of teduglutide to once per two days because of side effects at T12.

Conclusions: Teduglutide significantly reduced the weekly HPN volume at each time point (three, six and twelve months) and improved the patient-perceived health in this real-world data from Belgium. The effect of teduglutide started early after initiation, and was maintained over a longer period of time. These results are in line with previous real-world observations in other countries, with the unique advantage of including all adult patients treated with teduglutide in a single country.

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FREQUENT BUT GENERALLY MANAGEABLE BURDEN OF JAKNE WITH SEX-SPECIFIC PERSISTENCE IN UPADACITINIB-TREATED IBD: RESULTS FROM A LARGE SINGLE-CENTRE COHORT. V. Desmedt (1), E. De Dycker (1), T. Lambrechts (1), P. Geens (1), S. Brödel (1), E. Loddeijkx (1), J. Guedelha Sabino (1), M. Ferrante (1), T. Hillary (2), B. Verstockt (1) / [1] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Gastroenterology and Hepatology, [2] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Dermatology.

Introduction: Upadacitinib (UPA) is increasingly used for IBD, with acne reported more frequently in real-world cohorts than in trials. Evidence suggests this adverse event is relatively specific to UPA rather than other JAK inhibitors, yet its clinical course and management remain insufficiently defined.

Aim: We evaluated the prevalence, characteristics and outcomes of UPA-associated acne in a large single-centre cohort.

Methods: All patients initiating UPA for moderate-to-severe Crohn's disease (CD) or ulcerative colitis (UC) were prospectively followed at prespecified visits. Demographic, disease and treatment data were collected; acne cases were further assessed for timing, distribution, therapy, dose adjustment, dermatology referral and outcome. Logistic regression evaluated predictors of acne development and treatment needs. Uni and multivariate analyses were performed.

Results: We included 186 patients (63% male; median age 40.3 [IQR 29.3–50.7] years; 55% CD, with median follow-up of 0.59 [0.33–1.35] years. Acne occurred in 38.7% of patients. Patients with acne were numerically younger (37.3 vs 41.3 years; p=0.14), had shorter disease duration (9.3 vs 13.6 years; p=0.074) and slightly higher BMI (25.1 vs 24.2 kg/m²; p=0.23). Nicotine use was associated with lower acne risk (p=0.027). In multivariable analysis, age, disease duration, sex, IBD subtype, Montreal behaviour and location, and prior advanced therapy showed no significant association. Acne developed predominantly during induction (87.5%).

Facial involvement was common (68.1%), and truncal lesions (back and/or chest) occurred in 30.6%; neither distribution pattern was associated with treatment intensity or resolution. A structured dermatology protocol allowed on-demand treatment, with referral required in only 22.2% of patients. Topical therapy was required in 58.3% and systemic antibiotics in 20.8%. Maintenance dermatologic therapy (topical and/or systemic) was needed in 43.1%, and was strongly associated with female sex (72.4% vs 23.3%; $p < 0.001$). Resolution of acne during maintenance UPA dose was observed in 37.9%, with markedly higher rates in patients without need for ongoing dermatologic treatment beyond induction (48.8% vs 16.1%; $p = 0.006$). Only one patient (1.4%) discontinued UPA because of acne.

Conclusions: In the largest single-centre cohort reported, UPA-associated acne was substantially more common than in trials, but was usually manageable and rarely treatment-limiting. BMI modestly increased risk, and female sex predicted prolonged treatment need, while IBD phenotype and lesion distribution did not. These findings refine the clinical profile of JAKne and support proactive but reassuring monitoring during UPA therapy.

-I10-

EFFECT OF JAK INHIBITORS ON EXTRA-INTESTINAL MANIFESTATIONS AND CONCURRENT IMMUNE-MEDIATED INFLAMMATORY DISEASES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE. M. Truyens (1), P. Balestrieri (2), L. Pouillon (3), I. Psaroudakis (4), D. Ribaldone (5), I. Drygiannakis (6), A. Jauregui-Amezaga (7), C. Hedin (8), A. Todeschini (9), G. Mocci (10), K. Argyriou (11), X. Tolstoy (12), E. Shakweh (13), P. Ploutarchos (14), G. Calabrese (15), A. Blesl (16), I. Yudego (17), S. Vieujean (18), R. Filip (19), K. Karmiris (20), T. Taelman (21), H. Kani (22), M. García (23), A. Cremer (24), E. Savarino (25), C. Felice (26), H. Gordon (27), N. Vladimirova (28), M. Attauabi (29), M. Barreiro de Acosta (30), M. Georgios (31), T. Innocenti (32), T. Holvoet (33), M. Estevinho (34), T. Karakan (35), S. Vrakas (36), C. Kapizioni (37), N. Noor (38), G. Dagci (39), O. Nardone (40), J. Geldof (41), I. Koutroubakis (6), T. Lobatón Ortega (42) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology, [2] Fondazione Campus Bio-Medico, Rome, Italy, Gastroenterology Unit, [3] Imelda General Hospital, Belgium, Department of Gastroenterology and Hepatology, [4] Venizeleio General Hospital, Heraklion, Crete, Greece, Department of gastroenterology, [5] University of Turin, Italy, Department of Medical Sciences, [6] University Hospital of Heraklion, Crete, Greece, Department of Gastroenterology, [7] Antwerp University Hospital, Edegem, Belgium, Department of Gastroenterology and Hepatology, [8] Karolinska Institutet, Karolinska University Hospital, Sweden, Department of Gastroenterology, [9] IRCCS Sacro Cuore Don Calabria Hospital Negrar di Valpolicella, Verona, Italy, IBD unit, [10] Brotzu Hospital, Cagliari, Italy, Division of Gastroenterology, [11] General University Hospital of Larissa, Greece, Larissa, Greece, Department of Gastroenterology, [12] Karolinska Institutet, Karolinska University Hospital, Sweden, Department of Gastroenterology, Dermatovenereology and Rheumatology, [13] St Mark's National Bowel Hospital, United Kingdom, Department of Metabolism, Digestion and Reproduction, [14] University of Patras, Patras, Greece, Department of Internal Medicine, [15] University of Naples Federico II, Naples, Italy, Department of Clinical Medicine and Surgery, [16] Medical University of Graz, Graz, Austria, Department of Internal Medicine, [17] Hospital Universitario de Galdakao- Biobizkaia Health Research Institute, Spain, Servicio de Aparato Digestivo, [18] Clinique Saint-luc Bouge, Namur, Belgium, Hepato-gastroenterology Department, [19] University of Rzeszow, Rzeszów, Poland, Department of Internal Medicine, Faculty of Medicine, Collegium Medicum, [20] Venizelio General Hospital, Heraklion, Greece, Department of Gastroenterology, [21] AZ Groeninge, Kortrijk, Belgium, Department of Gastroenterology, [22] Marmara University Faculty of Medicine, Istanbul, Turkey, Department of Gastroenterology, [23] Universidad de Cantabria, Santander (Cantabria), Spain, Gastroenterology and Hepatology Department, Hospital Universitario Marqués de Valdecilla, Instituto de Investigación Sanitario Valdecilla (IDIVAL), [24] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Gastroenterology, [25] University of Padua, Padua, Italy, Gastroenterology Unit, [26] University Hospital Treviso, Treviso, Italy, Medicine 1 Unit, [27] Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom, Translational Gastroenterology Unit, [28] Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark, COPECARE, Copenhagen Centre for Arthritis Research, [29] Copenhagen University Hospital - Amager and Hvidovre, Denmark, Department of Gastroenterology and Hepatology, [30] Hospital Clinico Universitario de Santiago de Compostela, Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain, Department of gastroenterology, [31] General Hospital of Athens 'G. Gennimatas', Athens, Greece, Department of gastroenterology, [32] Careggi University Hospital, Florence, Italy, IBD Referral Centre, Clinical Gastroenterology Unit, [33] VITAZ, Sint-Niklaas, Belgium, Department of gastroenterology, [34] Unidade Local de Saúde Gaia Espinho, Vila Nova

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Introduction: Immune-mediated inflammatory diseases (IMIDs) and extra-intestinal manifestations (EIMs) are frequent in IBD and contribute substantially to morbidity. JAK inhibitors have demonstrated efficacy across several rheumatological IMIDs and emerging evidence suggests potential benefit in dermatological IMIDs such as atopic dermatitis.

Aim: To evaluate the effectiveness of JAK inhibitors on both IBD activity and associated EIMs/IMIDs in a large real-world international cohort.

Methods: This multicentric retrospective study was conducted within the framework of an ECCO National Study Group project (IMPACT-IBD). Adult patients with ulcerative colitis (UC) or Crohn's disease (CD) who initiated a JAK inhibitor (tofacitinib, upadacitinib or filgotinib) for IBD and had at least one EIM or IMID at baseline could be included. IBD and EIM/IMID activity were assessed after induction (week 6–14), at month 6 and at month 12 using physician's global assessment. IBD outcomes included clinical, biochemical (CRP <5mg/L and/or faecal calprotectin <250µg/g) and endoscopic remission. Treatment discontinuation due to primary non-response (PNR), loss of response (LOR) or surgery was classified as non-remission. The primary endpoint was EIM/IMID response while secondary endpoints included steroid-free IBD remission and new-onset of EIMs/IMIDs.

Results: A total of 214 patients were included: 122 with UC (57%) and 92 with CD (43%). Median age at JAK inhibitor initiation was 43 years (IQR 31–53), 53.1% were female (113/214), and median disease duration was 8 years (IQR 4–15). Prior IBD-related surgery had been performed in 36 patients (17%), almost exclusively in CD (33/92; 36%). The cohort was highly treatment-experienced: only 4 patients (1.9%) were naïve to advanced therapies, while 44 (21%) had received one, 84 (39%) two, and 81 (38%) three or more prior advanced treatments. Upadacitinib was the most frequently used agent (141/214; 66.4%), followed by tofacitinib (51/214; 23.8%) and filgotinib (21/214; 9.8%). Concomitant immunosuppression was prescribed in 29 patients (13.6%). Baseline disease activity was high, with clinical activity reported in 171/208 (82.2%) and endoscopic activity in 149/156 (95.5%) patients. The median CRP at baseline was 6.8 mg/L (IQR 1.9–20.8; n=192), and median faecal calprotectin was 545 µg/g (IQR 248.3–1564.5; n=114). At baseline, axial SpA was present in 94 and active in 68 (72.3%) patients, while peripheral SpA (including psoriatic arthritis) was present in 97 and active in 78 (80.4%). Dermatological IMIDs included psoriasis in 38 patients (active in 16/38; 42.1%), hidradenitis suppurativa in 9 (active in 8/9; 88.9%), erythema nodosum in 15 (active in 6/15; 40%), and pyoderma gangrenosum in 12 (active in 5/12; 41.7%). Uveitis was present in 15 patients (active in 1/15; 6.7%). Median follow-up was 10 months (IQR 5–12). Axial SpA showed response in 63/84 (75%) post-induction, 44/71 (62%) at month 6 and 25/44 (56.8%) at month 12. Peripheral SpA responded in 75/94 (79.8%) post-induction, 50/70 (71.4%) at month 6 and 35/49 (71.4%) at month 12. Psoriasis improved in 21/34 (61.8%) post-induction, 13/28 (46.4%) at month 6 and 8/20 (40%) at month 12. Hidradenitis suppurativa responded in 6/9 (66.7%) post-induction, 5/10 (50%) at month 6 and 3/6 (50%) at month 12. Improvement in erythema nodosum was seen in 9/16 (56.3%), 8/15 (53.3%) and 7/13 (53.8%) at the respective timepoints. Pyoderma gangrenosum responded in 8/11 (72.7%), 6/11 (54.5%) and 3/6 (50%). Uveitis improved in 8/16 (50%) post-induction, 9/14 (64.3%) at month 6 and 4/10 (40%) at month 12. Regarding intestinal outcomes, steroid-free clinical remission was achieved in 75/199 (37.7%) post-induction, 73/160 (45.6%) at month 6, and 63/116 (54.3%) at month 12. Steroid-free biochemical remission was reached in 116/187 (62%), 74/137 (54%) and 60/94 (63.8%); while steroid-free endoscopic remission was observed in 19/44 (43.2%), 21/49 (42.9%) and 26/49 (53.1%) at the respective timepoints. Among 170 patients with adequate follow-up, 7 (4.1%) developed a new EIM/IMID, including peripheral SpA (n=3), oral CD manifestations (n=2), pyoderma gangrenosum (n=1), axial SpA (n=1), primary sclerosing cholangitis (n=1) and autoimmune hepatitis (n=1). Treatment was discontinued in 62 patients (29%) after a median of 5 months (IQR 2–10), mainly due to active IBD (PNR: n= 14 (23%) or LOR: n=23 (37%)). Discontinuation due to worsening or new onset of EIMs/IMIDs occurred in 11 (18%) and 1 (2%) patient respectively.

Conclusions: JAK inhibitors demonstrated effectiveness for IBD activity and associated EIMs/IMIDs,

with particularly robust responses in peripheral SpA and more variable outcomes in dermatological manifestations. New-onset EIMs/IMIDs were uncommon.

-I11-

POSITIVE IMPACT OF A PSYCHOTHERAPEUTIC APPROACH BASED ON SOLUTION-FOCUSED BRIEF THERAPY ON FATIGUE, PSYCHOLOGICAL WELLBEING AND QUALITY OF LIFE IN INFLAMMATORY BOWEL DISEASE: A PROSPECTIVE SINGLE-CENTRE STUDY. J. Collin (1), L. Moor (1), L. Monin (1), P. Latour (1), C. Van Kemseke (1), S. Vieujean (1), E. Louis (1), C. Reenaers (2) / [1] CHU Liege, Liège, Belgium, Gastroenterology, [2] CHU Liège, Liège, Belgium, Gastroenterology.

Introduction: Fatigue affects 40–70% of patients with inflammatory bowel disease (IBD), including those in remission, yet few active interventions specifically target it. Solution-focused brief therapy (SFBT), is a short-term approach centred on patients' strengths and achievements rather than their difficulties. It promotes autonomy and engagement. The aim of this study was to assess the impact of SFBT on fatigue, anxiety, depression, sleep quality, and quality of life, and to identify predictors of response and adherence. **Aim:** The aim of this study was to assess the impact of SFBT on fatigue, anxiety, depression, sleep quality, and quality of life, and to identify predictors of response and adherence.

Methods: This was a prospective, interventional, single-centre, uncontrolled study conducted between January 2020–April 2024. IBD patients with fatigue (IBD-F score > 1), stable treatment for ≥3 months, and no corticosteroids were included. Fatigue and its impact were assessed using the IBD-F1 and IBD-F2 scores; anxiety and depression by the Hospital Anxiety and Depression Scale (HADS, score > 8 = positive); sleep quality by the Pittsburgh Sleep Quality Index (PSQI); and quality of life by the Subjective Happiness Scale (SHS). Stable psychotropic medication or ongoing psychiatric follow-up did not preclude inclusion. SFC was delivered by a single trained coach, with 3 to 6 sessions depending on patient progress. Adherence was considered complete when all sessions were attended, and null when discontinued after the first session. Dropouts were included in the adherence analysis.

Results: Sixty-seven patients were evaluated; six were referred for psychiatric care and eleven discontinued early (mean 1.6 sessions). Fifty patients were analysed: 68% female, median age 43 years (37–54), 65% with Crohn's disease. IBD-F1 scores significantly correlated with SHS ($r = 0.52$, $p < 0.0001$), PSQI ($r = 0.37$, $p = 0.0029$), and HADS ($r = 0.65$, $p < 0.0001$). SFBT significantly improved IBD-F1 ($p < 0.0001$), IBD-F2 ($p < 0.0001$), HADS ($p < 0.0001$), PSQI ($p = 0.0001$), and SHS ($p < 0.0001$) scores. Among 40 patients with HADS > 8, 15 (37.5%) responded: 7 improved on both dimensions, 5 on anxiety alone, and 3 on depression alone. Complete adherence was observed in 71.6% of participants; 11.9% discontinued after one session. Factors associated with reduced fatigue (IBD-F1) were female sex ($p = 0.017$), Montreal classification E1 vs E3 ($p = 0.009$), higher baseline IBD-F1 ($p = 0.025$), and lower body weight ($p = 0.010$). Reduction in fatigue impact (IBD-F2) was associated with higher HADS ($p = 0.012$), presence of perianal lesions ($p = 0.032$), and absence of clinical remission ($p = 0.001$). Better adherence was associated with absence of follow-up during the COVID period ($p = 0.035$), shorter disease duration ($p = 0.023$), use of anxiolytic/antidepressant medication ($p = 0.006$), psychiatric follow-up ($p = 0.001$), and higher baseline fatigue ($p = 0.017$).

Conclusions: SFBT appears to be a promising approach for managing fatigue in IBD. It significantly improves fatigue, anxiety, depression, sleep quality, and quality of life, even outside remission, particularly among women and patients with high baseline fatigue or anxiety. Controlled multicentre studies are warranted to confirm these findings and better define the patient profiles most likely to benefit from this integrative approach.

-I12-

HIGHER PERSISTENCE WITH SUBCUTANEOUS INFLIXIMAB COMPARED TO VEDOLIZUMAB IN STABLE INFLAMMATORY BOWEL DISEASE PATIENTS SWITCHING FROM MAINTENANCE INTRAVENOUS THERAPY CONFIRMED IN AN INDEPENDENT MULTICENTRE VALIDATION COHORT. A. Outtier (1), M. Truyens (2), L. Pouillon (3), F. Baert (4), A. Cremer (5), W. Van Moerkercke (6), A. D'Hooghe (7), T. Taelman (6), C. Liefferinckx (5), P. Bossuyt (3), T. Lobatón Ortega (2), M. Ferrante (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [2] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology, [3] Imelda General Hospital, Belgium, Imelda GI Clinical Research Centre, [4] AZ Delta, Belgium, Gastroenterology, [5] Erasme University Hospital -

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Introduction: Infliximab and vedolizumab are two biologic therapies used to treat patients with moderate-to-severe ulcerative colitis (UC) and Crohn's disease (CD). Initially, both therapies were marketed as intravenous (IV) infusions, but more recently, subcutaneous (SC) formulations became available. A previous single-centre study involving 140 patients who switched from maintenance intravenous (IV) to SC therapy reported higher treatment persistence with infliximab compared to vedolizumab: Outtier A, Hoffert Y, De Dycker E, et al. Treatment persistence, clinical, and biological outcomes following an elective switch from intravenous to subcutaneous infliximab and vedolizumab [abstract]. *J Crohns Colitis*. 2025;19(Suppl 1):i1431–i1432.

Aim: The current study aimed to validate higher treatment persistence with SC infliximab compared to vedolizumab in an independent cohort.

Methods: We conducted a multicentre retrospective study from May 2021 through January 2025 enrolling patients with inflammatory bowel disease (IBD) on maintenance IV infliximab or vedolizumab who switched to SC formulations with a minimum follow-up of 34 weeks. All patients had stable disease based on physician's global assessment. Demographics, disease characteristics, treatment history, and outcomes after switch were collected. The primary endpoint was SC treatment persistence. Secondary endpoints included reasons for treatment discontinuation and the need for SC dose escalation. A multivariate Cox proportional hazards model identified independent predictors of SC treatment discontinuation.

Results: A total of 400 patients (median [IQR] age 40.0 [30.3–53.0] y, 52.8% female, 39.5% UC, 60.5% CD, 46.5% infliximab, 53.5% vedolizumab) were included. None of the patients received concomitant steroids, while 28 patients (7.0%) used concomitant immunosuppressants (24 infliximab, 4 vedolizumab). Twenty-three percent of patients had elevated biomarkers (C-reactive protein >5 mg/L and/or faecal calprotectin >250 mg/kg) at switch. Optimized IV dosing was given to 37.1% of patients treated with infliximab, compared to 9.4% of patients treated with vedolizumab ($p < 0.001$). Thirteen patients (3.3%) initiated weekly SC dosing directly after switch (12 infliximab, 1 vedolizumab). Over a median (IQR) follow-up of 124 (76–160) weeks, 82.8% of patients remained on SC formulation (86.0% infliximab, 80.0% vedolizumab). Reasons for discontinuation were disease flare ($n=23$), adverse events ($n=20$), injection site reactions ($n=7$), disease remission ($n=7$), patient preference ($n=7$), non-compliance ($n=5$), and increased symptoms without objective signs of disease activity ($n=1$). Female sex (hazard ratio 1.93 [95% CI 1.15–3.23], $p=0.014$) and vedolizumab use (1.73 [1.02–2.93], $p=0.042$) were associated with SC treatment discontinuation. Forty-eight patients (12.0%) needed escalation to weekly SC dosing after switch (20 infliximab, 28 vedolizumab). Reasons for dose escalation were disease flare ($n=31$), increased symptoms ($n=14$), ongoing endoscopic disease activity ($n=2$), and subtherapeutic serum levels ($n=3$).

Conclusions: This multicentre validation cohort confirmed higher SC treatment persistence with infliximab compared to vedolizumab in stable IBD patients after switching from maintenance IV therapy. Discontinuation was mainly related to disease activity or adverse events, and was more frequent in women and vedolizumab users.

IMPACT OF PROACTIVE MEDICAL PROPHYLACTIC MANAGEMENT VERSUS A REACTIVE APPROACH ON LONG-TERM DISEASE RECURRENCE AFTER ILEOCECAL RESECTION FOR CROHN'S DISEASE. RESULTS OF AN EXPLORATORY EXTENSION OF THE PORCSE STUDY. J. Geldof (1), M. Truyens (2), M. Aelterman (2), K. Argyriou (3), A. Kapsoritakis (3), I. Bouchard (4), P. Rivière (4), D. Abrantes (5), J. Revés (5), J. Roseira (6), J. Cunha Neves (6), J. Nicholls (7), I. Arnott (7), A. Elorza (8), I. Rodríguez-Lago (8), R. Ferreiro-Iglesias (9), L. Nieto (9), P. Eder (10), T. Karakan (11), S. Dumanli (11), P. Bossuyt (12), L. Pouillon (12), V. Bouillon (13), A. Cremer (13), T. Holvoet (14), H. Peeters (15), S. Claeys (15), F. Baert (16), V. Desmedt (16), A. Jauregui-Amezaga (17), E. Van Dyck (18), T. Stroie (19), M. Diculescu (19), E. Theodoraki (20), I. Koutroubakis (20), M. Casanova (21), M. Mañosa Ciria (22), M. Cristiano (23), F. Portela (23), K. Karmiris (24), P. Nikolaou (24), S. Fernandes (25), I. Botto (25), L. Marquez Mosquera (26), F. Mesonero Gismero (27), T. Lobatón Ortega (28) / [1] University Hospital Ghent (UZ Gent), Ghent, Belgium, Gastroenterology and Hepatology (Maag- Darm- en Leverziekten), [2] Ghent University Hospital, Ghent, Belgium, Gastroenterology and Hepatology (Maag- Darm- en Leverziekten), [3] University Hospital of Larissa, Larissa, Greece, IBD Unit, Department of Gastroenterology, [4] CHU Bordeaux, France, Gastroenterology

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Introduction: The retrospective, multicentric, observational PORCSE study (Geldof et al. JCC. 2024.) evaluated postoperative recurrence of Crohn's disease after ileocaecal resection. Early medical prophylaxis (proactive strategy, cohort1) was found to have lower rates of endoscopic (Rutgeerts score >1) and clinical postoperative recurrence compared to expectant management (reactive strategy, cohort2) at first postoperative endoscopic evaluation.

Aim: In this analysis from a subgroup of the PORCSE population with extended follow-up duration, long term outcomes of the proactive vs reactive strategy after ileocaecal resection are explored.

Methods: A subgroup analysis was performed in patients with extended follow-up beyond the timeframe of the original PORCSE study. Primary endpoints were surgical (sPOR) and clinical (cPOR) recurrence. Endoscopic disease activity and progression were evaluated as secondary endpoints. Progression was defined as an increase in Rutgeerts score (>1) and/or development of colon inflammation from first to consecutive postoperative endoscopies. Logistic regression models with propensity score matching were fitted to adjust for confounding factors in comparing the proactive and reactive strategy.

Results: For 92.2% of the 346 originally included patients, a mean additional follow-up duration of 38.5 months (SD24.5) was available (mean total follow-up 110.9 months, SD44.8). sPOR and cPOR rate was numerically higher with the reactive strategy. However these differences were not statistically significant after correction for confounders (sPOR: cohort1: 13.2%, cohort2: 18.2%; OR 1.78, 95%CI 0.73-4.34, $P=0.202$ -cPOR: cohort1: 39.3%, cohort2: 49.7%; OR 1.73, 95%CI 0.92-3.24, $P=0.089$). No difference was found in IBD-related hospitalisation rate (cohort1: 10.8%, cohort2: 10.1%; OR 1.48, 95%CI 0.53-4.18, $P=0.457$). Survival analysis did not show a significant difference for time to sPOR (HR 1.34, 95% CI 0.59-3.06, $P=0.485$) nor in time to cPOR (HR 1.28, 95%CI 0.35-4.66, $P=0.713$). Rates of endoscopic disease activity (Rutgeerts >1 and/or colonic inflammation) at consecutive endoscopies after initial postoperative endoscopy did not differ between both strategies (cohort1: 59.2%, cohort2: 57.8%, OR 0.70, 95%CI 0.31-1.57, $P=0.381$). Univariate analysis revealed a higher rate of endoscopic progression with a proactive strategy (cohort1: 20.6%, cohort2: 10.6%, $P=0.041$). However, after correction for confounders this difference was no longer significant (OR 2.44, 95%CI 0.92-6.48, $P=0.073$).

Conclusions: In this large subgroup of patients with extended follow-up from the original PORCSE study, proactive medical prophylaxis after ileocecal resection showed no statistically significant differences compared with a reactive approach in reducing the rate of surgical and clinical postoperative recurrence, despite a numerical trend. Further prospective studies and larger cohorts are required to confirm these findings.

DISEASE VELOCITY IN INFLAMMATORY BOWEL DISEASE USING THE NEW IOIBD25 CLASSIFICATION: INSIGHTS FROM THE PANTHER COHORT. S. Verstockt (1), A. D’Hooghe (1), E. Glorieus (2), M. De Wolf (3), A. Cuvry (1), M. Lenfant (1), M. Truyens (2), J. Sabino (4), M. Ferrante (4), B. Hens (3), J. Geldof (5), D. Laukens (6), I. Cleynen (7), S. Vermeire (1), L. Vandermeulen (3), T. Lobatón Ortega (2), B. Verstockt (4) / [1] Translational Research Centre for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism, [2] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology, [3] University Hospital of Brussels, Brussels, Belgium, Department of Gastroenterology, [4] University Hospitals Leuven (UZ Leuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [5] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology, [6] Ghent University, Ghent, Belgium, Department of Internal Medicine and Paediatrics, [7] KU Leuven, Leuven, Belgium, Department of Human Genetics.

Introduction: The Montreal classification is widely adopted to classify inflammatory bowel disease (IBD), but does not fully capture disease progression. The newly proposed IOIBD25 classification introduces “disease velocity” as a central element.

Aim: This study evaluated the performance of this disease velocity component in a Belgian inception cohort.

Methods: The PANTHER cohort includes newly diagnosed adult patients with Crohn’s disease (CD) or ulcerative colitis (UC) from 3 Belgian IBD referral centres, enrolled within 3 months after diagnosis; and prior to any immunosuppressives, advanced therapies, or IBD-related surgery. Clinical data, including velocity events, were prospectively collected. Velocity, as defined by IOIBD25, was the time from diagnosis to first advanced therapy (T-class) or another predefined event (V-class), categorized as none (T0 or V0), ≥ 3 years (T1 or V1), 6 months–3 years (T2 or V2), and ≤ 6 months (T3 or V3). V-class events included hospitalization for acute severe flare or complication (UC: ASUC; CD: flare with fistula/abscess/obstruction), major surgery (UC: colectomy; CD: ileocecal, colectomy, or small-bowel resection), multi-refractory disease (≥ 3 advanced therapies), or high-grade dysplasia/colorectal cancer. Class patterns were assessed with alluvial plots, and time-to-event analyses with Kaplan–Meier methods. Candidate class cut-offs were identified through maximally selected rank statistics and grid-search with nested likelihood ratio tests (GraphPad Prism 10.3.0, R 4.3.2).

Results: Between 2015 and 2025, a total of 597 newly diagnosed patients were recruited, with a median (IQR) follow-up time of 3.6 (1.6–5.4) years. Of these, 270 patients (155 CD; 105 UC) had ≥ 3.5 years of follow-up and were included in the velocity analysis. The distribution of both T- and V-classes differed significantly between CD and UC (T: χ^2 $p = 1.24E-05$; V: χ^2 $p = 9.50E-06$). Early initiation of advanced therapy was common in CD (T3: 56%), whereas 17% remained without (T0). For other velocity events, 54% of CD patients remained event-free (V0) and 21% had a fast velocity (V3). In UC, early advanced therapy was less frequent (T3: 30%; T0: 42%); and most patients were event-free for V (V0: 81%). Combining T and V, a mild, event-free trajectory (T0V0) was found in 11% of CD and 42% of UC, while a successful top-down approach (T3V0) occurred in 29% of CD and 18% of UC. Time-to-event distributions suggested the need to refine the current velocity cutoffs: optimal T velocity cutoffs were identified at 0.5 and 1.6 years for CD, and at 1.0 and 3.3 years for UC, with two-cutoff models significantly outperforming single-cutoff models (Δ Akaike Information Criterion (AIC)=121 and 51, respectively; $p < 0.001$).

Conclusions: Incorporating disease velocity into IBD classification captures clinically meaningful heterogeneity in disease trajectories, as observed in this Belgian inception cohort. Refinement of the proposed time cut-offs of velocity events in real-world settings is warranted, and longer follow-up data will clarify how velocity-based classification informs disease modification assessment.

DISTINCT FATIGUE TRAJECTORIES IN ACTIVE IBD: CLINICAL PREDICTORS AND TREATMENT-LINKED IMPROVEMENTS INDEPENDENT OF INFLAMMATION. S. Rinckhout (1), T. Abts (1), F. Nasehi (2), M. Bourgery (2), L. Van Oudenhove (3), E. Vergaelen (4), M. Ferrante (5), J. Sabino (6), S. Schreiber (7), P. Rosenstiel (8), M. Van Den Houte (3), F. Tran (2), B. Verstockt (6) / [1] Translational Research Centre for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, IBD, [2] Christian-Albrechts-University and University Hospital Schleswig-Holstein, Kiel, Germany, Kiel, Germany, Institute of Clinical Molecular biology, Department of Internal Medicine I, [3] Translational Research Centre for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, LaBGAS, [4] University Psychiatric Centre, KU Leuven, Leuven, Belgium, Mind Body Research Group, [5] University Hospitals Leuven (UZ Leuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, KU Leuven, [6] University Hospitals Gasthuisberg, Leuven

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Introduction: Fatigue is one of the most debilitating and persistent symptoms in inflammatory bowel disease (IBD), often remaining despite adequate control of intestinal inflammation. Current treatments insufficiently address this burden, underscoring the need to better characterise its course and determinants.

Aim: The study aimed to identify distinct fatigue trajectories in patients with active IBD, and to determine clinical and psychological predictors of fatigue improvement over one year.

Methods: Data were derived from a large prospective cohort within the 3TR consortium, including 207 patients with active endoscopic ulcerative colitis (UC) or Crohn's disease (CD), recruited at 2 large referral centres. Assessments were performed at baseline, week 6 and 1 year after treatment initiation. Fatigue (FACIT-F), mental health (SF-36, mental component summary) and inflammatory markers (faecal calprotectin [FC] and C-reactive protein [CRP]) were collected at each visit. Latent class growth analysis (LCGA) was used to identify fatigue trajectory clusters based on intercepts and slopes of individual patients. Mixed-effects models tested the influence of advanced IBD treatment, baseline inflammation and mental health on fatigue changes.

Results: LCGA identified three distinct trajectories differing in fatigue severity ($p < 0.001$) at baseline with mild (FACIT-F=45.4), moderate (FACIT-F=28.6) and severe (FACIT-F=11) fatigue, with the majority (72.9%) of patients with active IBD in our cohort experiencing moderate-to-severe levels that often persist up to 1 year. The quadratic slopes over time did not significantly differ between the groups ($p > 0.05$), although patients with mild or moderate fatigue improved significantly, particularly in the first 6 weeks ($p < 0.01$), whereas those with severe baseline fatigue showed minimal change ($p = 0.51$; Figure 2A). Treatment with upadacitinib ($p < 0.001$), infliximab ($p < 0.001$) and vedolizumab ($p < 0.05$) was associated with greater fatigue improvement, while risankizumab ($p = 0.07$) and ustekinumab ($p = 0.15$) was not, despite similar baseline levels of fatigue (Figure 2B). Baseline mental health problems predicted worse initial fatigue, but greater improvement over time ($p < 0.05$; Figure 2C). Neither FC nor CRP at baseline were significantly associated with fatigue changes ($p = 0.53$).

Conclusions: LCGA identified three distinct fatigue trajectories, where the evolution appeared largely independent of baseline inflammatory activity. Improvement in fatigue was more strongly linked to specific advanced therapies and baseline mental health problems than baseline inflammatory markers. The differences between biologics classes are seen in a non-randomized setting and should lead to randomized controlled comparisons between interventions.

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EXTRACELLULAR MATRIX REMODELING AS A CONSEQUENCE OF BIOLOGIC THERAPY IN ULCERATIVE COLITIS. L. Giorio (1), K. Arnauts (1), M. Lenfant (1), W. Zadora (1), S. Abdurahiman (1), J. Sabino (2), M. Ferrante (2), S. Vermeire (1), B. Verstockt (2) / [1] Translational Research Centre for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, CHROMETA, [2] University Hospitals Leuven (UZ Leuven), Leuven, Belgium, Gastroenterology.

Introduction: IBD patients are continuously exposed to biological therapies, yet molecular consequences of prior biologic exposure on tissue characteristics and subsequent therapy response remain poorly understood. Considering the changing view of UC as a solely mucosal disease (1), and the higher treatment failure in biologic-experienced patients (2-3), an improved molecular understanding of disease phenotypes and the impact of therapy exposure is key.

Aim: In this study we explored whether bio-naïve and bio-experienced UC biopsies display distinct intrinsic molecular profiles.

Methods: Inflamed colonic biopsies ($e\text{Mayo} \geq 2$; $n=5$ bio-naïve, $n=5$ bio-experienced) were cultured ex vivo for 24 h (4) ($n=9/\text{patient}$), and subsequently RNA-sequenced (NovaSeq 6000; DESeq2). Gene co-expression networks were constructed using Weighted Gene Co-expression Network Analysis (WGCNA) on all samples to identify modules associated with biopsy traits ($\text{FDR} < 0.05$). Validation was performed in the TRIESTE-UC (5) cohort ($e\text{Mayo} \geq 2$; $n=15$ bio-naïve, $n=35$ bio-experienced).

Results: Comparison of bio-experienced versus bio-naïve UC biopsies revealed 860 up- and 497 downregulated genes, independent of ex vivo treatment. Bio-experienced samples showed enrichment of pathways linked to collagen biosynthesis, fibrosis, and extracellular matrix (ECM) organization, with TGFB1, AGT, RRAS2, and TWIST1 identified as top predicted upstream regulators ($z > 4.5$). WGCNA identified 20 co-expression

modules, of which the brown ($r=0.47$, $p=5.1\times10^{-5}$; ECM) and tan ($r=0.56$, $p=2.4\times10^{-7}$; angiogenesis/ECM) modules showed the strongest association with biologic exposure. Both modules were independent of disease duration, and interestingly, the tan module was uniquely associated with biologic exposure. Validation in the TRIESTE-UC (5) cohort confirmed enrichment of the bio-experienced gene signature ($FDR < 0.001$), and preservation of key WGCNA modules signatures ($FDR < 0.001$). Overlapping pathways and predicted upstream regulators in both cohorts, validated TGFBI and collagen pathway activation in the TRIESTE cohort. Similarly, hub genes from the tan module (RAI14, INHBA, ADAM12, TWIST1, RRAS2) were validated, and hierarchical clustering based on the tan module segregated most bio-experienced samples into a distinct molecular cluster in the independent validation cohort.

Conclusions: Our data reveal intrinsic molecular reprogramming in biologic-experienced UC, marked by persistent activation of ECM and fibrotic pathways independent of inflammation, disease duration, or ex vivo treatment. These findings underscore the need to re-think the definition of UC as a non-fibrotic disease (1). Recognizing therapy history as a molecular determinant is essential for interpreting treatment response and designing future translational and preclinical studies.

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TRANSCRIPTOMIC PROFILING REVEALS DIVERGENT MOLECULAR PATHWAYS UNDERLYING ULCERATIVE COLITIS DISEASE ACTIVITY AND PROGNOSTIC SEVERITY. A. D’Hooghe (1), S. Abdurahiman (2), S. Verstockt (2), L. Giorio (2), K. Arnauts (2), A. Cuvry (2), M. Ferrante (3), J. Sabino (3), S. Vermeire (2), B. Verstockt (3) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [2] KU Leuven, Leuven, Belgium, Translational Research Centre for Gastrointestinal Disorders (TARGID), [3] University Hospitals and Gasthuisberg, Leuven KU Leuven, Leuven, Belgium, Gastroenterology and Hepatology.

Introduction: Ulcerative colitis (UC) patients show substantial heterogeneity in inflammatory activity, treatment response and long-term disease severity. Endoscopic scores capture current inflammation, but not future disease trajectories. Identifying molecular mechanisms that distinguish various degrees of disease severity, may enable earlier prognostication and personalized disease trajectories.

Aim: This study examined transcriptomic differences between UC phenotypes to uncover molecular pathways and potential prognostic markers.

Methods: Inflamed (Mayo endoscopic sub score, $MES \geq 2$) mucosal colonic biopsies were obtained at diagnosis or prior to the first advanced therapy from 37 UC patients later failing ≥ 2 advanced therapies (S1), 50 UC patients with long-term remission (>2 years) after first-line advanced therapy (S2) and 16 UC patients with sustained remission with 5-ASA alone (S3). RNA sequencing was performed using Illumina NovaSeq X Plus. Weighted gene co-expression network analysis (WGCNA) was applied to identify phenotype-associated modules. Modules were deemed significant when the false discovery rate-adjusted value (p_{adj}) was below 0.05. Pathway enrichment of these modules was subsequently evaluated using Ingenuity Pathway Analysis (IPA) and Gene Set Enrichment Analysis (GSEA).

Results: Median age at diagnosis (interquartile range [IQR]) was generally lower in the S1 group (S1: 26 [21-4], S2: 31 [21-44], S3: 36 [29-46]) and more patients in the S3 group had proctitis (S1: 2.8%, S2: 14%, S3: 31%). Baseline MES were significantly higher in both S1 and S2 compared to S3 ($p=0.0013$; $p=0.037$). Multiple WGCNA modules correlated with MES, confirming a transcriptomic link to disease activity. None correlated with disease duration. However, two modules (M1 and M2) were uniquely upregulated in both S1 (M1: correlation [r] of 0.5, $p_{adj}=0.002$, M2: $r=0.3$, $p_{adj}=0.06$) and S2 (M1: $r=0.4$, $p_{adj}=0.006$, M2: $r=0.3$, $p_{adj}=0.02$) phenotypes, enriched for TNF α signalling (M1) and epithelial mesenchymal transition (EMT) (M2), suggesting shared tissue repair and inflammatory pathways. Predicted upstream regulators included TNF and EGF for M1, and SOX10 and WNT3A for M2. A distinct module, exclusively associated with S1 (M3: $r=0.3$, $p_{adj}=0.01$), showed strong enrichment in MYC targets genes and mitochondrial translation, protein import and degradation pathways, implicating dysregulated cell proliferation and survival. Key upstream regulators included HNF4A and IL3.

Conclusions: Although S1 and S2 show similarly high baseline inflammation, their long-term disease trajectories are shaped by distinct molecular programs, already in place before the first advanced therapy. EMT pathway activation may reflect beneficial tissue repair in responders but could contribute to fibrosis in refractory cases. MYC and mitochondrial pathways enrichment in S1 suggest a transcriptional signature of poor prognosis and treatment resistance. These findings underscore the importance of separating inflammatory activity from molecular severity, and may inform future biomarker development.

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UPADACITINIB RESTORES EPITHELIAL HOMEOSTASIS BY SUPPRESSING ER STRESS AND FIBROSIS IN UC. L. Giorio (1), K. Arnauts (1), C. Van de Perre (1), J. Sabino (2), M. Ferrante (2), S. Vermeire (1), B. Verstockt (2) / [1] Translational Research Centre for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, CHROMETA, [2] University Hospitals Leuven (UZ Leuven), Leuven, Belgium, Gastroenterology.

Introduction: Intestinal organoids provide a powerful tool to study epithelial responses in inflammatory bowel disease (IBD), preserving patient-specific and disease-relevant characteristics. As inflammation diminishes during culture, we previously developed inflammatory and endoplasmic reticulum (ER) stress-inducing cytokine mixes to mimic mucosal stress (1-2).

Aim: To study the direct epithelial effect of upadacitinib (UPA) – a JAK1 inhibitor – under inflammatory and ER stress conditions.

Methods: Ulcerative colitis (UC)-derived intestinal organoid (n=3, non-inflamed biopsies) were cultured in human expansion media (HM, 2 days), followed by differentiation media (DM, 4 days). From day 6, organoids were exposed for 48 hours to either DM only (control, CTRL), inflammation (INF: 50 ng/ml TNF α , 20 ng/ml IL1 β , 1 μ g/ml Flagellin) or ER stress (ER: 10 ng/ml TNF α , 20 ng/ml IL1 β , 1 μ g/ml Flagellin, 25 ng/ml Tunicamycin)(1). UPA (10 μ M) was administered for 48 hours (INF_UPA48, ER_UPA48), or the final 24 hours (INF_UPA24, ER_UPA24). Organoids were harvested on day 8 for RNA sequencing (Illumina NovaSeq 6000, DESeq2; Foldchange >1.5, FDR <0.05).

Results: Principal component (PC) analysis revealed clustering primarily by inflammatory treatment (PC1 28%, PC2 19.5%). In inflammatory settings, continuous UPA exposure (INF_UPA48 vs. INF) led to 103 differentially expressed genes (DEGS, 49 up, 54 down) including AKAP12, IFITM1, MFGE8, TJP1. Similarly, UPA supplementation in the final 24 hours (INF_UPA24), resulted in 8 DEGs (4 up, 4 down) including AKAP12, IFITM1, MFGE8, MX1. Under ER stress, 48 hours of combined UPA and ER exposure (ER_UPA48 vs. ER) altered 68 genes (20 up, 48 down) including MX1, MFGE8, IFITM1, EIF2AK2, while 24 hours exposure (ER_UPA24) affected 36 genes (7 up, 29 down) such as MX1, IFITM1, IFI44, MFGE8. Pathway analysis revealed strong downregulation of interferon (IFN) alpha/beta and gamma signalling, and modulation of host-responses in both ER_UPA conditions. Overlap across all UPA conditions, identified 4 genes consistently regulated by UPA, with greater transcriptional impact under ER stress. Across UPA-treated groups, JAK1 inhibition markers were downregulated, while MFGE8, encoding for a protein with both anti-inflammatory and antifibrotic properties (2), was upregulated. When INF was used as a trigger, UPA upregulated TJP1, a key marker of intestinal barrier restoration (3), while in the ER exposed condition EIF2AK2, an ER marker gene (4), was downregulated by UPA.

Conclusions: Upadacitinib exerts context-dependent epithelial effects that extend beyond immunosuppression, directly enhancing epithelial resilience and tissue restoration.

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DIETARY PATTERNS OF RECIPIENTS AND MICROBIAL RESTORATION IN ULCERATIVE COLITIS: INSIGHTS FROM THE RESTORE-UC TRIAL. S. Deleu (1), J. Vazquez Castellanos (2), M. Derrien (2), C. Caenepeel (1), S. Verstockt (1), K. Arnauts (1), E. Vissers (1), S. Proost (2), F. Baert (3), F. Mana (4), L. Pouillon (5), T. Lobatón Ortega (6), E. Louis (7), D. Franchimont (8), B. Verstockt (9), M. Ferrante (9), S. Vermeire (1), J. Raes (2), J. Sabino (9) / [1] Translational Research Centre for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Department of chronic diseases and metabolism, [2] Rega Institute, KU Leuven,

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Introduction: Rigorous donor preselection, strict anaerobic processing, and repeated faecal microbiota transplantation (FMT) administration did not improve outcomes for induction of clinical remission in the RESTORE-UC trial.

Aim: To better understand these results and inform future FMT trial designs, we investigated dietary patterns and fiber intake of recipients, and their associations with microbial composition, and ecosystem shift from dysbiosis.

Methods: The RESTORE-UC trial was a multi-centric double-blind, sham-controlled randomized trial. Patients with moderate to severe UC (total Mayo 4–10) were randomly allocated to receive four anaerobic-prepared allogenic or autologous donor FMTs. Food Frequency Questionnaires (FFQs) were collected at weeks 0 (n=62) and 8 (n=52) from recipients. From these, a population-specific diet health index was derived taking into account diet quality, equilibrium and diversity. Subsequently, k-means clustering was performed on daily intake of whole food groups. Quantitative microbiota profiling (QMP) was conducted on patient stool samples collected at weeks 0 (n=44) and 8 (n=44). We correlated dietary clusters and diet health scores with microbial genus abundances during induction phase (week 0 - 8). Clinical success was evaluated at week 8, including steroid-free clinical remission as well as clinical/endoscopic response (≥ 3 or $\geq 50\%$ reduction in combined Mayo subscores for rectal bleeding and stool frequency). Microbiota success was defined as enterotype shift with restoration of eubiosis (Bacteroides 2 (B2) to non-B2 enterotype), and other subtypes including no transition, non-B2 to other non-B2 transition, lead dysbiosis (non-B2 to B2), and maintenance of dysbiosis (B2 to B2).

Results: At week 8, patients restoring eubiosis showed a weak trend towards a higher percentage Dietary Health Index (%DHI) (Kruskal-Wallis; $p = 0.07$) and greater fiber intake per 1000 kcal ($p = 0.14$). Yet, no association with clinical success was found. K-mean clustering identified two main dietary patterns. Key whole food contributors to cluster separation include coffee with both sweeteners and sugar addition, alcoholic beverages, (all adj. $p < 0.05$), vegetables ($p < 0.01$; adj. $p = 0.06$) and brown bread ($p = 0.03$; adj. $p = 0.15$). Linear regression revealed modest associations between FFQ-derived intake and QMP genera, with effect sizes varying across both metadata and whole food variables.

Conclusions: This post-hoc analysis of the RESTORE-UC trial suggests that dietary improvements - particularly higher fiber intake - may enhance microbial restoration post-FMT. A lack of statistical power due to the limited number of clinical and microbial responders underscores the need for further investigation.

-I20-

EFFECT OF IL-23 INHIBITORS ON EXTRA-INTESTINAL MANIFESTATIONS AND CONCURRENT IMMUNE-MEDIATED INFLAMMATORY DISEASES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE. M. Truyens (1), O. Nardone (2), J. Geldof (3), X. Tolstoy (4), T. Lobatón Ortega (3), G. Calabrese (5), P. Balestrieri (6), A. Blesl (7), L. Pouillon (8), E. Shakweh (9), R. Filip (10), A. Todeschini (11), G. Mocci (12), D. Ribaldone (13), A. Jauregui-Amezaga (14), I. Yudego (15), S. Vieujean (16), T. Taelman (17), M. García (18), A. Cremer (19), E. Savarino (20), C. Felice (21), N. Vladimirova (22), M. Attauabi (23), M. Barreiro de Acosta (24), H. Peeters (25), T. Innocenti (26), T. Holvoet (27), A. Gutiérrez (28), M. Casanova (29), N. Noor (30), C. Hedin (31) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology, [2] University of Naples Federico II, Naples, Italy, Gastroenterology Unit, Department of Public Health, [3] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology, [4] Karolinska Institutet, Karolinska University Hospital, Sweden, Department of Gastroenterology, Dermatovenereology and Rheumatology, [5] University of Naples Federico II, Naples, Italy, Department of Clinical Medicine and Surgery, [6] Fondazione Campus Bio-Medico, Rome, Italy, Gastroenterology Unit, [7] Medical University Graz, Graz, Austria, Department of Internal Medicine, [8] Imelda General Hospital, Belgium, Department of Gastroenterology and Hepatology, [9] St Mark's National Bowel Hospital, United Kingdom, Department of Metabolism, Digestion and Reproduction, [10] University of Rzeszow, Rzeszów, Poland, Department of Internal Medicine, Faculty of Medicine, Collegium Medicum, [11] IRCCS Sacro Cuore Don Calabria Hospital Negrar di Valpolicella, Verona, Italy, IBD unit, [12] Brotzu Hospital, Cagliari, Italy, Division

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Introduction: Immune-mediated inflammatory diseases (IMIDs) and extra-intestinal manifestations (EIMs) are frequent in IBD and contribute substantially to morbidity. In recent years, IL-23 inhibitors have shown efficacy in IBD and in dermatological IMIDs such as psoriasis, while their benefit in rheumatological manifestations, particularly axial spondyloarthritis (SpA), appears limited.

Aim: To evaluate the effectiveness of IL-23 inhibitors on IBD activity and associated EIMs/IMIDs in a real-world international cohort.

Methods: This multicentric retrospective cohort study was conducted within the framework of an ECCO National Study Group project (IMPACT-IBD). Adult patients with ulcerative colitis (UC) or Crohn's disease (CD) who initiated risankizumab, mirikizumab or guselkumab for IBD and who had at least one EIM or IMID at baseline could be included. IBD and EIM/IMID activity were assessed after induction (week 6–14), at month 6 and at month 12 using physician's global assessment. IBD outcomes included clinical, biochemical (CRP <5mg/L and/or faecal calprotectin <250µg/g) and endoscopic remission. Treatment discontinuation due to primary non-response (PNR), loss of response (LOR) or surgery was classified as non-remission. The primary endpoint was EIM/IMID response while secondary endpoints included steroid-free IBD remission and new-onset of EIMs/IMIDs.

Results: A total of 83 patients were included (13 UC, 16%; 70 CD, 84%), with a median follow-up duration of 6 months (IQR 3–10). Median age was 46 years (IQR 34–58), 53% were female and median disease duration was 11 years (IQR 4–23.5). Prior IBD-related surgery had been performed in 34 patients (42.5%), exclusively in those with CD. The cohort was highly treatment-experienced: 2 patients (2.4%) were naïve to advanced therapies, 21 (25.6%) had received one, 22 (26.8%) two and 37 patients (45.1%) three or more prior advanced treatments. Risankizumab was used in 68/83 patients (81.9%), mirikizumab in 10/83 (12%) and guselkumab in 5/83 (6%), and concomitant immunosuppression was prescribed in 18 patients (21.7%). Baseline IBD activity was substantial, with clinical activity in 61 patients (78.2%), and endoscopic activity in 61/64 (95.3%). The median CRP at baseline was 4.1 mg/L (IQR 1.2–12; n=73), and median faecal calprotectin was 470.5 µg/g (IQR 109.5–905.8; n=48). At baseline, axial SpA was present in 22 patients and active in 13 (59.1%), while peripheral SpA (including psoriatic arthritis) was present in 26 and active in 21 (80.8%). Dermatological IMIDs included psoriasis in 33 patients (active in 23/33; 69.7%), hidradenitis suppurativa in 14 (active in 6/14; 42.9%), erythema nodosum in 5 (active in 0/5), and pyoderma gangrenosum in 1 (active in 0/1). Uveitis was present in 5 patients (active in 0/5). Axial SpA responded in 7 of the 15 assessed patients (46.7%) after induction, 5/8 (62.5%) at month 6 and 3/7 (42.9%) at month 12. Throughout follow-up, a worsening of axial SpA occurred in 4/22 patients (18.2%). Peripheral SpA responded in 11/19 (57.9%) after induction, 12/18 (66.7%) at month 6 and 5/10 (50%) at month 12. Psoriasis improved in 14 of the 27 assessed patients (51.9%) after induction, 12/17 (70.6%) at month 6 and 7/10 (70%) at month 12. Hidradenitis suppurativa responded in 5/11 (45.5%) after induction, 5/9 (55.6%) at month 6 and 1/2 (50%) at month 12. Regarding intestinal outcomes, steroid-free clinical remission was achieved in 17 of 71 assessed patients (23.9%) after induction, 21/45 (46.7%) at month 6 and 12/25

(48%) at month 12. Steroid-free biochemical remission was reached in 36/70 (51.4%), 20/41 (48.8%) and 12/23 (52.2%) at the respective timepoints. Steroid-free endoscopic remission rates were 5/19 (26.3%), 2/7 (28.6%) and 6/11 (54.5%) post-induction, at month 6 and 12 respectively. Among 58 patients with available follow-up data, 4 (4.1%) developed new-onset EIMs or IMIDs. These included 2 cases of peripheral SpA and 1 case each of psoriasis and uveitis. In 9 patients (10.8%) treatment was discontinued after a median of 8 months (IQR 4.3-10.8). Multiple reasons for treatment discontinuation could be selected and included the following: worsening of the pre-existing EIM/IMID (n=5), LOR (n=3), PNR (n=1) and new onset EIM/IMID (n=1).

Conclusions: IL-23 inhibitors demonstrated effectiveness for IBD activity and psoriasis and achieved response rates of approximately 50% in hidradenitis suppurativa, axial and peripheral SpA. New-onset EIMs/IMIDs were uncommon. Interpretation of these outcomes remains limited due to small subgroup sizes, and further studies are needed to better define the role of IL-23 inhibition in IBD patients with coexisting IMIDs.

-I21-

SUBCUTANEOUS INFLIXIMAB IN IBD PATIENTS PREVIOUSLY TREATED WITH AN OPTIMIZED INTRAVENOUS INFLIXIMAB DOSING SCHEDULE: BASELINE CHARACTERISTICS LINKED TO WILLINGNESS TO SWITCH. T. Holvoet (1), A. Moens (2), J. Sabino (3), P. Bossuyt (4), T. Lobatón Ortega (5), A. Cremer (6), C. Caenepeel (7), A. Posen (8), C. Thienpont (9), B. Willandt (10), L. Capircchio (11), A. Amezcaga (12), G. Lambrecht (13), F. Baert (14), N. Deprez (15), H. Peeters (16), C. Reenaers (17), S. Vanden Branden (18), J. De Rechter (19), I. Arijns (19), E. Dreesen (20), B. Belgian IBD Research and Development (21), M. Ferrante (3) / [1] Vitaz, Sint-Niklaas, Belgium, Gastroenterology, [2] Heilig Hartziekenhuis Lier, Lier, Belgium, Gastroenterology, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [4] Imelda Hospital, Bonheiden, Belgium, Gastroenterology, [5] Universitair ziekenhuis Gent, Belgium, Gastroenterology, [6] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology, [7] Ziekenhuis Oost-Limburg (ZOL), Genk, Belgium, Gastroenterology, [8] AZ Vesalius Tongeren, Tongeren, Belgium, Gastroenterology, [9] ZAS, Antwerp, Belgium, Gastroenterology, [10] AZ Sint-Jan Brugge, Brugge, Belgium, Gastroenterology, [11] Centre Hospitalier Wallonie Picarde (CHWAPI), Tournai, Belgium, Gastroenterology, [12] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology, [13] AZ Oostende, Oostende, Belgium, Gastroenterology, [14] AZ Delta, Belgium, Gastroenterology, [15] AZ Maria Middelaers, Ghent, Belgium, Gastroenterology, [16] AZ Sint-Lucas, Ghent, Belgium, Gastroenterology, [17] CHU Liege, Liège, Belgium, Gastroenterology, [18] AZORG AALST, Aalst, Belgium, Gastroenterology, [19] BIRD Office, Belgium, BIRD, [20] KUL - University of Leuven, Leuven, Belgium, Department of Pharmaceutical and Pharmacological Sciences, [21] Belgian IBD Research and Development (BIRD), Belgium, BIRD.

Introduction: Subcutaneous (SC) infliximab (IFX) CT-P13 offers an alternative to intravenous (IV) administration, yet evidence remains limited regarding its use in patients maintained on optimized IV dosing (1).

Aim: The ongoing AMARETTO trial (NCT06113913) aims to investigate whether switching to weekly SC IFX 120 mg is associated with better outcomes compared to bi-weekly SC administrations in patients with inflammatory bowel disease (IBD) receiving optimized IV therapy. This analysis examines the baseline patient characteristics linked to willingness to switch from optimized IV to SC IFX and explores patient-reported reasons for (not) switching.

Methods: This Belgian multicentre, randomized, open-label superiority trial includes adult IBD patients treated with optimized IV IFX who are in steroid-free clinical and biological remission. Remission was defined as: (1) no corticosteroid exposure within the preceding eight weeks; (2) PRO-2 based on last 3 days before study visit with rectal bleeding score of 0 and stool frequency score of ≤ 1 for ulcerative colitis (UC)/IBD unclassified (IBDU), or average daily abdominal pain score of ≤ 1 and a liquid stool frequency score of ≤ 2.8 for Crohn's disease (CD); and (3) C-reactive protein (CRP) <10 mg/L, faecal calprotectin <250 $\mu\text{g/g}$. Eligible patients could either continue optimized IV IFX (IV comparison group) or switch to SC IFX. Those choosing SC were randomized 1:1 to open-label weekly (SC intervention) or bi-weekly 120 mg SC IFX (SC comparison). The primary endpoint is the proportion of patients maintaining steroid-free clinical and biological remission at week 52 without treatment optimization. This analysis focuses on two secondary outcomes: (1) baseline characteristics associated with willingness to switch to SC, and (2) patient's reported motivations for or against switching. Between-group comparisons were performed using

Mann-Whitney U-test for continuous variables and Fisher's exact/Chi-square test for categorical variables (GraphPad Prism 10.6.1), with $p < 0.05$ considered statistically significant.

Results: Patient recruitment is complete, with 275 patients enrolled between May 2024 and October 2025 (149 patients switching to SC and 126 continuing IV). Baseline characteristics were comparable between those willing and unwilling to switch. No significant differences were observed in sex distribution, smoking status, IBD subtype (CD/UC/IBDU), disease duration, disease extent or behaviour, presence of extra-intestinal manifestations, use of combination therapy with an immunomodulator, first-line use of IFX, duration of IFX therapy, duration of current optimized IV dosing, or corticosteroid use in previous year. The only characteristic associated with willingness to switch was age. Patients who opted for SC IFX were significantly younger than those choosing to continue their IV therapy (median age interquartile range [IQR] 36 years [29-51] vs. 43 years [30-58]; $p = 0.03$). When examined across age groups, willingness to switch decreased with increasing age: 59.2% for ages 18–29 ($n = 76$), 60.2% for ages 30–40 ($n = 68$), 51.5% for ages 41–54 ($n = 66$), and 44.6% for ages 55–80 ($n = 65$) (Chi-square test for trend, $p = 0.03$). Patient-reported reasons for switching were primarily practical. The most common motivations were: anticipated reduction in hospital visits (89/149, 60%), time gain (86/149, 58%), greater independence from the hospital (23/149, 11%), altruistic research motivation (6/149, 3%), and difficulties with IV administration (6/149, 3%). Among patients not willing to switch, the main concerns were fear of change (65/126, 52%), fear of disease relapse (30/126, 24%), fear of potential non-adherence (12/126, 10%), reduced contact with health care professionals (9/126, 7%), and needle aversion (8/126, 6%).

Conclusions: Apart from younger age being associated with greater willingness to switch, baseline characteristics did not differ between willing or unwilling to switch from optimized IV to SC IFX. Motivations for switching were mainly practical, reflecting a desire in reduced hospital visits and time savings, while reluctance was primarily driven by fear of change and concerns about disease control. The AMARETTO trial will further clarify whether weekly SC dosing offers superior outcomes compared to bi-weekly SC IFX in this population.

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CLINICAL BENEFITS OF SWITCHING FROM USTEKINUMAB TO A SELECTIVE IL23 P19 INHIBITOR IN PATIENTS WITH ENDOSCOPIC DISEASE ACTIVITY (SHELTER). M. Ferrante (1), D. Beeckmans (2), S. Brams (3), M. Nigro (2), E. Eggermont (4), J. Sabino (1), S. Vermeire (1), B. Verstockt (1) / [1] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Gastroenterology, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, gastroenterology, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [4] Translational Research Centre for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism CHROMETA.

Introduction: In clinical practice, patients with inflammatory bowel disease (IBD) not achieving endoscopic remission with the IL12/23 p40 inhibitor ustekinumab (UST) may be switched to an IL23 p19 inhibitor. This therapeutic transition is based on clinical trial data suggesting that p19 inhibitors are more potent in achieving endoscopic endpoints.

Aim: We aim to explore the effects of switching from UST to commercially available selective p19 inhibitors in patients with ongoing endoscopic disease activity.

Methods: We included adult patients with Crohn's disease (CD) or ulcerative colitis (UC), who were treated with subcutaneous UST 90mg every four or every eight weeks and this for at least 16 weeks and switched to a p19 inhibitor due to ongoing endoscopic disease activity [Simplified Endoscopic Score for Crohn's Disease (SES-CD) >5 for CD (SES-CD >3 for isolated ileitis) or endoscopic Mayo score (EMS) ≥ 2 for UC]. All patients had at least one year of follow-up and underwent endoscopy at baseline and after one year of the selected p19 inhibitor treatment. Patients with an ostomy, an ileal pouch-anal anastomosis, or prior exposure to a p19 inhibitor were excluded. The primary endpoints were the evolution of the endoscopic scores (SES-CD, the EMS, or the ulcerative colitis Endoscopic Index of Severity (UCEIS)), based on Wilcoxon Signed-Rank testing. We also evaluated endoscopic remission in CD, defined as a SES-CD ≤ 4 with at least a 2-point reduction from baseline, and no sub-score >1 (SES-CD ≤ 2 for isolated ileitis), and endoscopic improvement in UC, defined as an endoscopic Mayo score of 0 or 1. The weighted PRO2 score for CD was calculated as (liquid/very soft stool frequency $\times 2$) + (abdominal pain $\times 5$). PRO2 clinical remission for CD was defined as an abdominal pain score ≤ 5 and liquid/very soft stool frequency (SF) score ≤ 3 . The PRO2 score for UC was calculated by combining the SF and rectal bleeding (RB) scores. SF

normal; RB score: 0 = none; 1 = streaks of blood <50% of stools; 2 = obvious blood most of the time, 3 = only blood is passing. PRO2 clinical remission for UC was defined as a SF score of 0 and RB score ≤ 1 .

Results: As of 20 November 2025, 54 patients were switched from UST to a p19 inhibitor of whom 33 patients had at least one year of follow-up and fulfilled all eligibility criteria. A total of 26 patients with CD [12 men; median (interquartile range, IQR) age 46 (41-62) years; nine patients in PRO2 clinical remission; 13 patients treated with UST 4-weekly] were included. One year after initiating a p19 inhibitor (all risankizumab), the median (IQR) SES-CD score dropped numerically from 7 (5-8) to 5 (4-8) ($p=0.12$). Five CD patients (19%) achieved endoscopic remission after one year. One patient with CD [female, 71 years old, treated with UST 8-weekly] had to switch to an alternative therapy due to persisting debilitating symptoms after 24 weeks. A total of seven patients with UC [3 men; median (IQR) age 45 (38-53) years; three patients in PRO2 clinical remission; two patients treated with UST 4-weekly] were included. One year after switching to a p19 inhibitor (all mirikizumab, four patients with extended intravenous induction), the median (IQR) EMS and UCEIS scores dropped significantly from, respectively, 2 (2-3) to 1 (0-2) ($p=0.026$) and 3 (3-4) to 0 (0-2) ($p=0.017$). Five UC patients (71%) showed endoscopic improvement after one year of treatment. The maintenance scheme of UST was not a predictive variable for endoscopic remission, endoscopic improvement or PRO2 clinical remission (all $p>0.05$).

Conclusions: Considering the relatively small sample size, a clear trend of endoscopic improvement was observed in patients with IBD one year after switching from UST to a selective IL23 p19 inhibitor. This SHELTER cohort will further be expanded.

-I23-

MATERNAL AND NEONATAL OUTCOMES IN WOMEN WITH INFLAMMATORY BOWEL DISEASE FOLLOWING DIFFERENT BIOLOGIC UTILIZATION TRAJECTORIES IN PREGNANCY. E. De Dycker (1), E. Van den Broeck (2), Z. Annaert (3), P. Geens (1), T. Lambrechts (1), E. Loddewijx (1), S. Brödel (1), K. Van Calsteren (4), L. Lannoo (4), J. Guedelha Sabino (1), M. Ceulemans (2), B. Verstockt (1), M. Ferrante (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [2] KUL - University of Leuven, Leuven, Belgium, Pharmaceutical and Pharmacological Sciences, [3] KUL - University of Leuven, Leuven, Belgium, Faculty of Pharmaceutical Sciences, [4] KUL - University of Leuven, Leuven, Belgium, Development and Regeneration.

Introduction: Inflammatory bowel disease (IBD) often affects women of reproductive age. Maintaining disease control in the perinatal period is crucial to avoid adverse outcomes. The 2025 Global Consensus guideline recommends continuing biologics throughout pregnancy. However, more real-world data on biologic use patterns during pregnancy and associated outcomes are needed.

Aim: Our goal was to evaluate maternal and neonatal outcomes in pregnant women with IBD across different biologic treatment trajectories.

Methods: A retrospective study was performed using medical records from pregnant women with IBD, treated and/or delivering at our tertiary centre between 2017 and 2025. Disease activity in pregnancy was a composite variable based on the notification of clinical worsening, initiation of IBD medication, and/or delivery due to disease activity in the medical record. Patients were categorized into four groups based on biologics utilization in pregnancy: continuers, discontinuers, initiators or non-users.

Results: In total, 255 pregnancies were included: 103 were continuers (66 CD, 37 UC), 68 discontinuers (47 CD, 21 UC), 7 starters (4 CD, 3 UC) and 77 non-users (44 CD, 32 UC, 1 IBD type unclassified). Maternal age at conception was similar across continuers (30.9 years), discontinuers (30.6 years), initiators (29.7 years), and non-users (30.7 years). Before conception, 67.1% used biologics, exclusively among continuers and discontinuers. Disease activity during pregnancy was highest among initiators (100.0%), followed by discontinuers (27.9%), continuers (22.3%) and non-users (19.5%). Biologics were typically discontinued or initiated around 22 weeks' gestation. Mean gestational age at delivery was 38 weeks 5 days. Preterm birth (<37 weeks) occurred most in initiators (14.3%), then discontinuers (12.1%), continuers (8.1%) and non-users (3.2%). Mean birthweight was lowest in initiators (2999 g) and highest in non-users (3366 g). Low birthweight (<2500g) was more frequent in initiators (14.3%), followed by continuers (9.3%), discontinuers (6.0%) and non-users (1.6%). In contrast, small for gestational age was most common in continuers (18.9%), followed by initiators (14.3%), discontinuers (9.0%) and non-exposed women (7.9%). C-section rates were highest in non-users (41.3%) and discontinuers (39.4%) compared to continuers (31.5%).

Conclusions: In this cohort from a specialized IBD clinic, women who discontinued biologics during

score: 0 = normal number of stools; 1 = 1–2 more than normal; 2 = 3–4 more than normal; 3 = ≥ 5 more than pregnancy had higher rates of preterm birth, C-sections, and third-trimester disease activity compared to continuers, supporting the potential benefits of maintaining biologic therapy during pregnancy. However, the higher rate of SGA infants among continuers may reflect confounding by indication and warrants further research. All initiators presented with disease activity and had the highest rates of preterm birth and section, underscoring the importance of adequate disease control during pregnancy.

-I24-

OPTIMIZING COLONOSCOPY TIMING IN IBD USING MULTIMODAL AI INTEGRATING UR-CARE. S. Louis (1), N. Lembrechts (1), K. Van Brantegem (2), I. El Idrissi (1), L. Pouillon (1), P. Bossuyt (1) / [1] Imelda Hospital, Bonheiden, Belgium, Gastroenterology, [2] Imelda Hospital, Bonheiden, Belgium, IT Department.

Introduction: Patients with colonic inflammatory bowel disease (IBD) are at increased risk for colorectal cancer (CRC). Regular surveillance is essential for early detection of dysplastic lesions and prevention of malignant transformation. Determining the optimal timing for surveillance colonoscopies is complex and depends on multiple factors such as disease activity and extent, comorbidities, and co-occurrence of primary sclerosing cholangitis (PSC). We aimed to develop an AI algorithm that integrates data from multiple sources to automatically indicate the optimal timing of colonoscopy follow-up in individual patients with IBD, supporting timely clinical planning.

Aim: To develop and implement a guideline-based AI algorithm that integrates multimodal clinical and patient-reported data to automatically determine the optimal timing of surveillance colonoscopy in patients with colonic IBD.

Methods: We created an algorithm based on international guidelines for IBD CRC surveillance. The clinical, endoscopic and microscopic variables feeding the algorithm are extracted from multiple structured data sources including the hospital electronic medical record (EMR), the UR-CARE local database and coded pathology reports. To address data gaps, an annual digital questionnaire is distributed through the hospital app to collect additional details requiring regular updates (e.g. family history of CRC). This information is then integrated to maintain up-to-date personalized recommendations.

Results: Automated feeding of a colonoscopy surveillance algorithm is feasible using structured data input sources and leads to personalized colonoscopy timing recommendations. In case of incomplete data, the system automatically paused at the relevant decision point, prompting a precautionary recommendation for an earlier colonoscopy to ensure patient safety and maintain decision accuracy. To ensure prompt intervention and appropriate follow-up care, the output of the AI-tool is displayed on the patient's individual monitoring dashboard and an automated red flag notification system alerts clinicians when a patient is due for a follow-up within the next year.

Conclusions: The implementation of an AI-assisted, guideline-based algorithm provides an innovative, standardized and efficient framework for determining colonoscopy intervals in IBD surveillance. By combining structured clinical data and patient-reported updates, the system enhances the precision and timeliness of CRC prevention. The real-time dashboard visualization and red flag alerts support proactive patient management. A prospective study comparing the AI-based recommendations with the current standard of care is planned to evaluate its full clinical impact.

-I25-

ADDRESSING ELEVATED CLEARANCE IN CHRONIC POUCHITIS: A POPPK-PD-GUIDED USTEKINUMAB DOSING STRATEGY. W. Zhang (1), A. Outtier (2), O. Dewit (3), E. Louis (4), M. Ferrante (2), E. Dreesen (1) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Pharmaceutical and Pharmacological Sciences, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Department of Gastroenterology, [4] CHU Liege, Liège, Belgium, Department of Gastroenterology.

Introduction: Off-label ustekinumab benefits patients with chronic pouchitis, yet its pharmacokinetics (PK) and target concentrations remain unclear.

Aim: We aimed to characterize its population PK in chronic pouchitis, identify concentration thresholds predicting clinical remission (modified pouchitis disease activity index < 5 and a reduction by ≥ 2 points), and propose optimized dosing regimens.

Methods: Twenty-two patients with chronic pouchitis were included. All received standard ustekinumab intravenous induction dosing (~6 mg/kg), followed by 90mg subcutaneous maintenance dosing every eight weeks. Serum samples were collected at week (w)4, w8, w16, and w24. A population pharmacokinetics (popPK) model was developed to characterize ustekinumab PK. A population pharmacodynamics (popPD) model using logistic regression was used to link drug concentrations and clinical remission and to identify the cutoff. Monte Carlo simulations (n=1000) were conducted for the 22 patients comparing four induction dosing strategies: (1) standard label dosing, (2) exact 6 mg/kg, (3) 6 mg/kg rounded to the nearest 130 mg vial size, and (4) increased fixed-dose regimen (390 mg <55 kg, 520 mg 55–85 kg, 650 mg >85 kg). For each strategy, the rate of target attainment was calculated based on the identified cutoff.

Results: The PopPK model well captured the time course of ustekinumab concentrations. Standardized to a 70-kg patient with albumin level 44 g/L, clearance (CL) was estimated at 0.348 L/day. The popPD model identified w4 drug concentrations as a predictor of clinical remission at w16, with a threshold of 15.0 mg/L (AUC 0.84; 95% CI 0.62–1.00). Simulations revealed that standard dosing achieved this target exposure in only 46.6% of patients (95% CI 46.0–47.3). An exact 6 mg/kg dosing improved this to 57.0% (95% CI 56.4–57.7), while vial-rounded dosing further increased target attainment to 60.9% (95% CI 60.3–61.6). The increased fixed-dose regimen achieved the highest target rate at 80.2% (95% CI 79.6–80.7). Notably, the vial-rounded dosing strategy provided consistent exposure across weight bands (58.6% <55 kg; 61.4% 55–85 kg; 60.4% >85 kg), mitigating underexposure in lighter patients (<55 kg), who had a target rate of only 10.4% under the standard regimen.

Conclusions: Clearance of ustekinumab in patients with chronic pouchitis is 1.5–2 times higher than that in Crohn's disease and ulcerative colitis. W4 concentrations were predictive of clinical remission at w16, with a cutoff of 15.0 mg/L. The vial-rounded induction strategy substantially improves target attainment, particularly in the lighter patients.

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MUCIN RNA ISOFORM EXPRESSION AND ITS ASSOCIATION WITH CLINICAL SEVERITY SCORES AND BARRIER GENE NETWORKS IN ULCERATIVE COLITIS. B. Oosterlinck (1), J. Gassman (1), A. Jauregui-Amezaga (2), M. Somers (2), J. De Man (1), B. De Winter (1), A. Smet (1) / [1] University of Antwerp, Antwerp, Belgium, LEMP, [2] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology and Hepatology.

Introduction: Mucosal healing is a key therapeutic endpoint for ulcerative colitis (UC) patients and is defined as endoscopic improvement and histological remission without taking barrier healing into account. Mucins are critical components of the mucosal barrier that give rise to structurally diverse isoforms. Recently, we reported mucin mRNA isoforms capturing patient heterogeneity and barrier function.

Aim: Here, we explored the relationship between clinical scoring systems (i.e. patient reported outcomes, PRO2; Ulcerative Colitis Endoscopic Index of Severity, UCEIS; Mayo Endoscopic Score, MES; Geboes scores) in UC patients and mucin mRNA isoforms, as well as their correlation with barrier-related genes.

Methods: RNA from colonic biopsies of UC patients (27 non-inflamed; 36 inflamed) and healthy controls (n=35), was sequenced. Reads were mapped to our mucin isoform landscape using Kallisto and analysed with Sleuth. The PRO2, UCEIS, MES, and Geboes scores were categorised into four bins: no disease, mild, moderate, severe. Associations between scores and mucin RNA isoforms were assessed using multinomial regression. The correlations with barrier-related genes were also assessed.

Results: When considering the PRO2 score, an increased expression of the MUC1 (ENST00000462317.5), MUC4 (PB.1238.363) and MUC16 (ENST00000397910.8) RNA isoforms was observed in UC patients with mild and moderate disease. Expression of MUC16 (ENST00000397910.8) was increased in patients with mild to severe disease as defined by the MES scoring whereas an increased expression of MUC4 (PB.1238.363) and decreased expression of MUC5B (PB.2816.52) and MUC20 (PB.1239.830) significantly associated with moderate and severe scores. Regarding the UCEIS scores, expression of MUC16 (ENST00000397910.8) was increased in UC patients with mild to moderate disease but decreased in patients with severe disease activity. Altered expression levels of MUC4 (PB.1238.363), MUC5B (PB.2816.52) and MUC20 (PB.1239.830) associated with moderate Geboes scores. Correlation analysis ($|r| \geq 0.5$, $p < 0.05$) revealed strong associations between barrier-related genes and MUC1 (ENST00000462317.5), MUC20 (ENST00000447234.7), MUC4 (PB.1238.363), and MUC5AC (PB.2811.15), and to a lesser extent with MUC20 (PB.1239.830) and MUC5B (PB.2816.52). The above mentioned MUC1, MUC4, and MUC5AC isoform expressions positively correlated with JAK2 expression; the MUC4 isoform also with JAK1 and

STAT3 and the MUC1 isoform with STAT1 and STAT3.

Conclusions: Distinct mucin RNA isoforms are associated with disease activity and key barrier-related genes (e.g. JAK/STAT pathways), further supporting their potential for monitoring mucosal healing.

-I27-

SCREENING OF AVOIDANCE/RESTRICTIVE FOOD INTAKE DISORDER (ARFID) IN PATIENTS WITH QUIESCENT INFLAMMATORY BOWEL DISEASE IRRITABLE BOWEL SYNDROME-LIKE SYMPTOMS. P. Van Ouytsel (1), A. Cremer (1), D. Franchimont (1), C. Liefferinckx (1), L. Amininejad (1), H. Piessevaux (2), H. Louis (1), C. Vuckovic (1) / [1] Hôpital Erasme, ULB, Belgium, Gastroenterology, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Brussels, Belgium, Gastroenterology.

Introduction: Inflammatory bowel diseases (IBD) are chronic immune-mediated disorders of the gastrointestinal tract characterised by alternating periods of remission and relapse. Even in the absence of active inflammation, patients with quiescent disease frequently report symptoms consistent with irritable bowel syndrome (IBS), which may lead to restrictive dietary patterns and ultimately increase the risk of Avoidant/Restrictive Food Intake Disorder (ARFID).

Aim: The aim was to evaluate the prevalence of patients at risk of ARFID among patients with quiescent IBD and IBS-type symptoms, and to evaluate association between the risk of ARFID and the FODMAP consumption.

Methods: A cross-sectional study was performed from February 2025 to September 2025 on adult IBD patients whose recent work-up showed endoscopic and biological remission as per STRIDE II criteria. Self-administered questionnaires (SCOFF-F, NIAS-Fr, FFQ-FODMAPs-BE, BSS, GAD-7, PHQ-9, IBS SSS, PRO-2, HBI) were completed remotely via REDCap. Univariate and multivariate logistic regression were performed, with the significant threshold fixed at 5%.

Results: Sixty-two patients were enrolled (65% female, 66% Crohn's disease, mean age 39±14 years). Overall, 16 patients (26%) screened positive for ARFID risk. Among these 16 patients, the distribution across subscales (picky eater, small appetite, fear of eating) was as followed: 63% (10/16) fulfilled one subscale, 31% (5/16) fulfilled two subscales, 6% (1/16) fulfilled all three. Higher IBS symptom severity was associated with a higher risk of positive screening for ARFID. In a multivariate logistic regression model, positive screening for risk of ARFID was associated with mild FODMAP consumption (FFQ-FODMAP-BE <1.80) and anxiety.

Conclusions: One in four patients with quiescent IBD has a positive screening for ARFID. Anxiety and low FODMAP intakes are the main determinants of positive screening. These findings support the need for integrated psychological and dietetic assessment in IBD patients presenting functional gastrointestinal symptoms.

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REAL-WORLD MONITORING PRACTICES IN IBD: INSIGHTS FROM THE BELGIAN COHORT OF THE MULTI-COUNTRY IBD-PODCAST STUDY. B. Verstockt (1), P. Bossuyt (2), A. Colard (3), F. D'Heygere (4), J. Van Dongen (5), A. Despeghel (6), C. Semanaz (6), D. Franchimont (7) / [1] University Hospitals Leuven (UZ Leuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] Imelda Hospital, Bonheiden, Belgium, Department of Gastroenterology, [3] Clinique MontLégia, CHC Groupe Santé, Liège, Belgium, Department of Gastroenterology, [4] AZ Groeninge, Kortrijk, Belgium, Department of Internal Medicine, [5] AZ Sint Maarten, Mechelen, Belgium, Department of Gastroenterology, [6] Abbvie, Wavre, Belgium, Medical, [7] Erasme Hospital, Brussels, Belgium, Department of Gastroenterology.

Introduction: Effective monitoring in inflammatory bowel disease (IBD) is central to the treat-to-target approach endorsed by international guidelines, aiming to optimize outcomes through early identification of disease activity using non-invasive biomarkers and subsequent intervention. However, real-world adoption of these practices in Belgium is not well characterized.

Aim: The IBD-PODCAST study aimed to estimate the proportion of patients with IBD with suboptimal disease control (SDC) according to STRIDE-II. This analysis describes real-world IBD monitoring practices in Belgium and compares them with international practices and guideline recommendations.

Methods: IBD-PODCAST was a cross-sectional, non-interventional study including patients with ulcerative colitis (UC) and Crohn's disease (CD) from 10 countries conducted between February 2022 and February 2023. SDC was assessed based on pre-defined indicators from the STRIDE-II recommendations. Retrospective data were collected on treatment history, endoscopy and imaging performed within

the previous 12 months, alongside biomarker assessments within 14 days of the index visit. This analysis examined utilization rates of biomarkers, endoscopy, and imaging modalities for monitoring. **Results:** The multi-country cohort (n=2,185) consisted of 1,108 patients with CD and 1,077 with UC, with a mean (SD) disease duration of 12.9 (9.6) years and 11.9 (8.8) years, respectively. The Belgian cohort included 75 patients with CD and 57 with UC, with a mean (SD) disease duration of 15.1 (11.6) years and 12.9 (8.0), respectively. SDC was observed in 46.7% (35/75) of Belgian patients with CD compared to 52.2% (578/1108) in the multi-country CD cohort, and in 42.1% (24/57) of Belgian patients with UC compared to 44.3% (477/1077) in the multi-country UC cohort. FC was measured in 20.0% (15/75) of Belgian patients with CD versus 22.5% (249/1108) in the multi-country CD cohort, and in only 5.3% (3/57) of Belgian patients with UC versus 22.8% (246/1077) in the multi-country UC cohort. CRP was the most frequently measured biomarker, tested in 62.7% (47/75) of Belgian patients with CD, compared to 54.3% (601/1,108) in the multi-country CD cohort. For UC, 54.4% (31/57) of Belgian patients and 52.1% (561/1,077) of the multi-country cohort underwent CRP testing. Endoscopy was performed in 40.0% (30/75) of Belgian patients with CD, compared to 33.4% (370/1,108) of patients in the multi-country CD cohort. Among patients with UC, 56.1% (32/57) of Belgian patients underwent colonoscopy as opposed to 39.6% (426/1,077) in the multi-country cohort. Non-invasive imaging techniques, including magnetic resonance imaging/enterography (MRI/E), computed tomography (CT), and ultrasound, were infrequently performed overall. MRI/MRE was conducted in 8.0% (6/75) of Belgian patients with CD versus 9.0% (100/1,108) in the multi-country CD cohort, and MRI/CT was performed in 7.0% (4/57) of Belgian patients with UC compared to 3.0% (32/1,077) in the multi-country UC cohort. Ultrasound was performed in 9.3% (7/75) of Belgian patients with CD compared to 8.0% (89/1,108) in the multi-country CD cohort, and in 1.8% (1/57) of Belgian patients with UC versus 7.2% (77/1,077) in the multi-country UC cohort.

Conclusions: Real-world IBD monitoring practices in the Belgian cohort were largely consistent with those observed in the multi-country cohort, though distinctions emerged, particularly in FC utilization and frequency of endoscopic evaluation in patients with UC. FC testing was underutilized in CD in Belgium, consistent with the multi-country cohort. Despite its role as the most sensitive biomarker in IBD, FC testing was underutilized in UC in Belgium, likely due to reimbursement limitations and patient reluctance. CRP testing was widely adopted and conformed to guideline recommendations across both cohorts and indications. Although Belgian patients demonstrated better disease control, they underwent endoscopy more frequently overall, with a greater disparity observed in patients with UC relative to the multi-country cohort. This greater reliance on endoscopic evaluation may be related to its requirements for reimbursement of advanced therapies and restricted access to FC testing. Utilization of MRI/E, CT, and ultrasound was limited, reflecting current guidelines, though ultrasound is gaining recognition as a cost-effective non-invasive monitoring tool. The persistently low uptake of FC testing, together with relatively high endoscopy rates in UC, highlights a critical gap in biomarker-driven disease monitoring in Belgium. Overcoming barriers to FC test reimbursement and broader adoption could help Belgium better align with evidence-based guidelines and reduce dependence on invasive procedures in UC. Study limitations include the short monitoring window, as biomarker measurements were reported only within 14 days of the index visit.

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INTESTINAL ULTRASOUND ACTIVITY CORRELATES WITH IBD-RELATED DISABILITY SCORES IN PATIENTS WITH ULCERATIVE COLITIS BUT NOT IN CROHN'S DISEASE
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Introduction: Patient-reported outcomes and non-invasive monitoring tools play a pivotal role in monitoring inflammatory bowel disease (IBD). The IBD-Disk provides a standardized evaluation of IBD-related disability, a key long-term outcome that captures patients' functional well-being (Ghosh et al. *Inflamm Bowel Dis.* 2017). Intestinal ultrasound (IUS) is a reliable, non-invasive modality to evaluate disease activity in Crohn's disease (CD) and ulcerative colitis (UC), but its link to patient-reported disability remains uncertain.

Aim: The aim of this study is to examine the relationship between intestinal ultrasound activity, assessed using the International Bowel Ultrasound Segmental Activity Score (IBUS-SAS), and IBD-related disability, measured by the IBD-Disk.

Methods: This retrospective study included IBD patients with paired IUS assessments and IBD-Disk questionnaires completed within one week. UC patients with isolated proctitis were excluded. IUS

activity was quantified using the the IBUS-SAS, with a cutoff of 23 for UC (Innocenti et al. J Crohns Colitis. 2025) and 25.2 for CD (Dragoni et al. J Crohns Colitis. 2023). Statistical analyses included Spearman correlations, Wilcoxon tests, ROC curves, and mixed-effects models for longitudinal data. **Results:** Forty-nine UC patients were included (34% female, 71% left-sided colitis, median [interquartile range] age 37.0 [30.0-53.0] years, disease duration 7.0 [1.0-12.0] years), with 15 having repeated assessments. UC patients with high IBUS-SAS had significantly higher IBD-Disk scores than those with low IBUS-SAS ($p < 0.001$). IBUS-SAS correlated moderately with total IBD-Disk ($\rho = 0.389$, $p = 0.006$) and with several subcomponents, including abdominal pain ($\rho = 0.300$, $p = 0.0362$), defaecation regulation ($\rho = 0.451$, $p = 0.0011$), social interaction ($\rho = 0.405$, $p = 0.0039$), education and work ($\rho = 0.481$, $p = 0.0005$), energy ($\rho = 0.318$, $p = 0.0258$), and emotions ($\rho = 0.356$, $p = 0.012$). A weak correlation was observed with sexual function ($\rho = 0.294$, $p = 0.040$). No significant correlations were found with sleep, body image, or joint pain. Mixed-effects modelling showed a stable association over time (interaction $p = 0.89$). ROC analysis identified an optimal IBD-Disk cutoff of 41.5 (AUC 0.80, 95% CI 0.66-0.94; sensitivity 79%, specificity 80%). Sublayer analysis showed submucosal thickness correlated with defaecation regulation ($p = 0.414$, $p = 0.04$), but not with total IBD-disk or other domains. Ninety-seven CD patients were included (54.6% female, 61.9% isolated ileal disease, median age 39.0 [27.0-54.0] years, disease duration 8.0 [2.0-18.0] years). No significant difference in IBD-Disk scores was found between high and low IBUS-SAS groups ($p = 0.06$). IBUS-SAS correlated weakly with total IBD-Disk ($p = 0.208$, $p = 0.041$), with inconsistent subcomponent correlations. ROC analysis showed poor discrimination (AUC 0.62, 95% CI 0.50-0.74; sensitivity 46%, specificity 78%). **Conclusions:** IUS-defined disease activity correlates significantly with patient-reported disability in UC, with stable longitudinal associations, suggesting IUS reflects clinically relevant disease burden and may complement endoscopic and clinical assessments. In CD, this relationship is weaker and inconsistent, likely reflecting heterogeneous clinical presentations and the complex transmural nature of CD, highlighting the need for multimodal assessment tools combining IUS with additional outcome measures to capture disease burden.

-I30-

BIO-EXPERIENCED STATE DRIVES DIFFERENTIAL RESPONSES TOWARDS GLPG3970 IN EX VIVO BIOPSIES FROM PATIENTS WITH ULCERATIVE COLITIS. K. Arnauts (1), L. Giorio (1), M. Colli (2), F. Kolb (3), S. De Vos (4), J. Guedelha Sabino (5), M. Ferrante (5), S. Vermeire (1), B. Verstockt (5) / [1] Translational Research Centre for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism, [2] Aspect Analytics NV, Genk, Belgium, Aspect Analytics NV, [3] Onco3R Therapeutics BV, Heverlee, Belgium, Onco3R Therapeutics BV, [4] FoxBioPath BV, Duffel, Belgium, FoxBioPath BV, [5] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: GLPG3970 targeted inhibition of salt-inducible kinases (SIK) 2/3 combines anti-inflammatory and immunoregulatory activity. (1,2) GLPG3970 showed positive effects on histology, endoscopy and faecal calprotectin in a 6-week phase 2a signal-detection study, consistent with preclinical findings of pro-inflammatory cytokines suppression and goblet cell protection, although without differentiation from placebo for total Mayo Clinic Score. (2-5).

Aim: Building on our previous ex vivo comparison of GLPG3970 with approved UC therapy tofacitinib, (6) this study aimed to elucidate the mechanistic effects of GLPG3970 and delineate response patterns in bio-naïve and bio-experienced patients.

Methods: Inflamed UC biopsies (bio-naïve $n = 5$, bio-experienced $n = 5$; endoscopic sub-Mayo ≥ 2) were treated ex vivo for 24 h with GLPG3970 (60 μM), vehicle, or tofacitinib (10 μM), followed by supernatant profiling (V-PLEX 54-plex) and bulk transcriptomics by Illumina NovaSeq 6000 (Salmon + DESeq2; FoldChange > 1.5 , FDR < 0.05). Weighted gene co-expression analysis (WGCNA) was run on DMSO and GLPG3970 samples only along Gene ontology (GO) pathways, with multiple testing correction (FDR < 0.05). RNA-protein correlation was assessed in matched samples (Log₂FC, Spearman R, p-values).

Results: GLPG3970 exposure significantly reduced pro-inflammatory cytokine (TNF α , GM-CSF, IFN- γ) and chemokine (MCP-1, MIP1 α , MIP1 β) release in supernatant, as well as transcriptomic activity of NF- κ B driven inflammatory mediators (e.g. CSF2, MMP9, CCL4), and pathways including antigen presentation, collagen formation and inflammasome signaling. Transcriptomic and proteomic responses were strongly correlated ($R = 0.70$, $p = 1.3 \times 10^{-7}$), while GLPG3970 exposure could partially reverse a UC transcriptomic disease signature (7) ($\rho = -0.25$). WGCNA identified 18 gene expression modules, 7 of which were significantly associated with bio-experienced status [turquoise (extracellular structure and remodelling; $r = 0.58$, FDR

3.6x10⁻⁵; green module (r=0.34, FDR 0.031)]. Upon GLPG3970 exposure, the green module correlation was reversed (r=-0.41, FDR 0.028) encompassing angiogenesis, cell motility and connective tissue pathways with TGFB1 identified as central hub gene. Modulation of this and the purple module – linked to RNA and mRNA processing - was driven by bio-experienced patients, and absent in bio-naïve patients.

Conclusions: GLPG3970 effectively suppressed inflammatory signaling in UC ex vivo biopsies. Network analysis showed enhanced extracellular remodeling in bio-experienced patients, with GLPG3970 reversing connective tissue-related processes in this group. These findings emphasize the importance of considering prior treatment exposure in patient stratification and preclinical study design.

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REUVOLUTION-IBD: PREVALENCE OF MUSCULOSKELETAL SYMPTOMS IN EARLY INFLAMMATORY BOWEL DISEASE: FIRST INTERIM RESULTS OF A SINGLE CENTRE PROSPECTIVE COHORT STUDY. E. Martens (1), J. Geldof (2), M. Truyens (2), F. Van den Bosch (3), D. Elewaut (3), G. Varkas (3), T. Lobatón Ortega (2) / [1] Universiteit Gent, Gent, Belgium, Faculty of Medicine, [2] Ghent University Hospital, Ghent, Belgium, Gent, Belgium, Department of Gastroenterology, [3] Ghent University Hospital, Ghent, Belgium, Gent, Belgium, Department of Rheumatology.

Introduction: IBD patients have an increased risk of developing extraintestinal manifestations. Although EIMs are a known phenomenon, the available data is heterogeneous in methodology and employed definitions. Recently, very high prevalences of musculoskeletal (MSK) symptoms have been described by Vladimirova et al (1).

Aim: The aim of this cohort is to evaluate the prevalence and evolution of EIMs in early IBD patients and to identify risk factors associated with the development of rheumatic and musculoskeletal diseases (RMDs).

Methods: Newly diagnosed (<1 year) (Cohort A) and/or bio-naïve (Cohort B) IBD patients were included since April 2024 at the outpatient clinic from a tertiary IBD centre. Patients underwent endoscopic evaluation and received standard of care treatment by their IBD physician. At baseline, every IBD patient underwent a comprehensive rheumatological work-up including a full clinical and biochemical evaluation, as well as MRI of the axial skeleton and HLAB27 testing. Interim results after 1 year of study recruitment are reported. Statistics were performed using SPSS statistics 31. Data distribution was assessed for normality and appropriate descriptive statistics were applied accordingly.

Results: So far, a total of 37 patients were included. The mean age of all patients was 35.5 years old (SD 10.2) of whom 20 (54.1%) were male and 23 (62.2%) were diagnosed with Crohn's disease. Twenty-two patients (59.5%) experienced MSK symptoms. The mean age of onset for axial symptoms was 27.8 years old (SD 11.1 [11.8;57.8]) and the median duration of symptoms between onset and IBD diagnosis was 2.4 years (IQR 11.8). The mean age of onset for peripheral symptoms was 31.5 years old (SD 9.4 [19.5;45.8]). The median time between onset and IBD diagnosis was 0.8 years (IQR 3.4). The median BASDAI score for all patients at baseline was 1.8 (IQR 2.0) indicating a low overall subjective burden of inflammatory MSK symptoms in this cohort. Three patients (8.1%) were diagnosed with axial spondyloarthritis(axSpA) after rheumatological evaluation at baseline. All three were male, had Crohn's disease and presented with MSK symptoms. Strikingly, the mean ASDAS score for these 3 patients was only 1.25 (SD 0.27 [0.86; 1.76]), which corresponds with inactive disease in axSpA. No other significant differences in MSK symptoms when comparing ulcerative colitis vs Crohn's disease, Cohort A vs B, were found. No significant associations between MSK symptoms and IBD disease activity indicators were observed.

Conclusions: First interim results of the REUvolution IBD study show a high prevalence of MSK symptoms

in bio-naïve IBD patients, in accordance with recent literature. Nevertheless, only 13.6% of those with symptoms were diagnosed with an underlying RMD. Therefore, caution is warranted when interpreting reports on MSK symptoms in IBD trials.

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DISEASE DURATION IMPACTS IMMUNE SIGNATURES IN BIOPSIES FROM PATIENTS WITH ULCERATIVE COLITIS. K. Arnauts (1), L. Giorio (1), M. Lenfant (2), W. Zadora (1), S. Abdurahiman (1), J. Guedelha Sabino (2), M. Ferrante (2), S. Vermeire (1), B. Verstockt (2) / [1] Translational Research Centre for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Associations between disease duration and achieving remission are well established in Crohn's disease (CD), but remain unclear in ulcerative colitis (UC)(1-3). At the molecular level, oxidative phosphorylation and mitochondrial dysfunction have been linked to prolonged disease duration in CD, but not in UC (4).

Aim: The aim of this study is to understand molecular changes throughout the disease course to refine patient stratification and uncover pathways driving (sub)mucosal remodeling.

Methods: Inflamed colonic biopsies (eMayo ≥ 2 ; n=5 bio-naïve, n=5 bio-experienced) were cultured ex vivo for 24h(5) (n=9/patient), subsequently RNA-sequenced (NovaSeq 6000; DESeq2), and analysed by Ingenuity Pathway Analysis (IPA) and cell type enrichment analysis by xCell(6). Gene co-expression networks were identified via Weighted Gene Co-expression Network Analysis (WGCNA) (FDR >0.05) on all samples. Validation used active controls from the TRIESTE-UC cohort (n=24; eMayo ≥ 2 ; split by disease duration <2.5 or >10 years(7)).

Results: Co-expression analysis of ex vivo biopsies identified 20 gene modules linked to distinct traits. Two modules - red ($p=6.2 \times 10^{-11}$) and cyan ($p=2.1 \times 10^{-5}$) – were negatively correlated with disease duration, independent of prior biological exposure. Both were enriched for immune regulatory pathways, including reduced “T cell activation” and “adaptive immune response” with longer disease duration. In contrast, the turquoise module ($p=0.048$), associated positively with metabolic processes in disease duration. Cell type enrichment highlighted an overall reduced ImmuneScore, and reduced B- and T-cell type enrichment– in longer disease duration (FDR <0.001), while hierarchical clustering segregated samples with long disease duration. Notably, endoscopic activity did not correlate with any of these modules. Validation using GSEA in the TRIESTE cohort confirmed a negative enrichment score (ES -0.65) for downregulated genes from the discovery cohort, and the red module ES (-0.66), while the cyan module showed a mild negative ES (-0.29). BANK1 was a leading-edge gene in the validation cohort (Log2FC -1.51, FDR 0.012; discovery Log2FC -2.29, FDR 5.93×10^{-19}), and red module hubs IKZF1 (Log2FC -0.66; FDR 0.116) and IKZF3 (Log2FC -0.883; FDR 0.117) showed similar downregulation trends.

Conclusions: We identified reduced T cell, B cell, and adaptive immunity signatures in UC biopsies with longer disease duration, independent of inflammation or biological exposure. Key regulators included IKZF1/3– drivers of Th17-Treg plasticity(8) - and BANK1, which modulates B cell-Treg interactions(9). These findings highlight altered immune regulation along disease progression and suggest opportunities for duration-tailored therapeutic.

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-I33-

COMPLEMENTARY AND ALTERNATIVE MEDICINES USE IN IBD AND THE NEED FOR MULTIDISCIPLINARY CARE: PROSPECTIVE DATA FROM A TERTIARY CENTRE. L. Khrouz (1),

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Introduction: Inflammatory bowel disease (IBD) is a chronic inflammatory condition of the gastrointestinal tract that significantly affects quality of life (QoL) through both intestinal and extra-intestinal manifestations. As patients seek to alleviate persistent symptoms such as fatigue, chronic pain, and psychological distress, the use of complementary and alternative medicines (CAMs) has increased. In parallel, multidisciplinary teams (MDTs) integrating psychological and nutritional expertise may play an important role in addressing the multifaceted burden of IBD.

Aim: This study aimed to explore the use of CAMs among IBD patients followed at a Belgian tertiary centre, to identify factors associated with their use, and to assess patients' perspectives on implementing MDTs to support integrative care.

Methods: This prospective study was conducted between December 2024 and March 2025, following ethics committee. All adult IBD patients were eligible. CAM use was assessed via anonymized questionnaires based on the validated I-CAM-Q questionnaire covering several domains including dietary habits, physical activity, psychotherapy, and addictions. Statistical analysis included descriptive statistics, Chi-square or Fisher's exact tests for categorical variables, and Mann-Whitney U test for continuous variables.

Results: Of the 460 questionnaires distributed, 242 were analysed (169 Crohn's disease (CD), 73 ulcerative colitis (UC)). The cohort showed markers of severe disease: 50% of CD patients had undergone ≥ 1 surgery and most patients (both CD and UC patients) were treated with advanced therapies (biologics or JAK inhibitors). Three-quarters ($n = 181$) reported satisfactory QoL under conventional IBD management. Overall, 40% ($n = 90$) reported using CAMs, yet only 41.4% of them ($n = 36$) disclosed this to their gastroenterologist. CAM use was associated with higher educational level ($p = 0.003$), but not with age, gender, IBD subtype, or disease duration. Patients with unsatisfactory QoL were more likely to use CAM ($p = 0.007$), and 54.2% of CAM users ($n = 45$) reported improved QoL. The most frequent CAMs were physical activity (59.1%, $n = 123$), vitamins (57.6%, $n = 117$), pre- and/or probiotics (29.1%, $n = 55$), mindfulness (24.1%, $n = 49$), psychotherapy (23.5%, $n = 48$), and dietitian consultations (22.2%, $n = 42$). Physical activity was primarily practiced for overall well-being, while pre- and/or probiotics and dietitian consultations were mainly used for the management of IBD-related symptoms. Physical activity was more frequently reported by UC vs CD patients (71.7% vs 53.7%, $p = 0.017$) and was associated with higher education level ($p = 0.003$). QoL improvement was associated with physical activity ($p = 0.004$), vitamins ($p < 0.001$), pre- and/or probiotics ($p < 0.001$), mindfulness ($p < 0.001$), and psychotherapy ($p = 0.012$). The majority of IBD patients (87.0%, $n = 188$) supported the development of MDTs, an opinion associated with CAM use ($p = 0.003$) and CAM-related QoL improvement ($p = 0.035$). In particular, 69.0% ($n = 150$) were in favour integrating psychologists and dietitians in their care.

Conclusions: CAM use is frequent among IBD patients in tertiary care, especially among those reporting lower perceived QoL. While physical activity was the most used and performed for general well-being, pre-/pro-biotics were mostly used for the management of IBD-related symptoms. Despite frequent use and reported benefits, discussion about CAMs with gastroenterologists remains limited underscoring potential gaps in safety monitoring and shared decision-making. The strong patient support for MDTs reflects unmet psychological and nutritional needs with standard follow-up. These findings emphasize the relevance of integrating multidisciplinary, holistic approaches into IBD management.

EVALUATING FACTORS ASSOCIATED WITH HOSPITALISATIONS, EMERGENCY VISITS AND RELATED COSTS IN INFLAMMATORY BOWEL DISEASE THROUGH THE TRUECOLOURS-IBD DIGITAL MONITORING PROGRAMME IN OXFORD. L. Fierens (1), P. Clarke (2), G. Dunbar (3), A. Kormilitzin (4), L. Matini (3), A. Punj Sharda (3), S. Travis (5), A. Walsh (6), M. Violato (2) / [1] KU Leuven, Leuven, Belgium, Translational Research Centre for Gastrointestinal Disorders (TARGID), Department of Chronic Diseases, Metabolism, and Ageing, [2] University of Oxford, Oxford, United Kingdom, Nuffield Department of Population Health, [3] University of Oxford, Oxford, United Kingdom, Nuffield Department of Medicine, [4] University of Oxford, Oxford, United Kingdom, Department of Psychiatry, [5] University of Oxford, Oxford, United Kingdom, Kennedy Institute of Rheumatology, [6] Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom, Translational Gastroenterology Unit - John Radcliffe

Hospital.

Introduction: Remote monitoring in inflammatory bowel diseases (IBD) may help identify patients at risk of higher healthcare use. The TrueColours-IBD (TC-IBD) system, initiated at the Oxford University Hospitals in 2018, enables patients to report baseline case mix variables, weekly symptoms (HBI for Crohn's disease (CD); SCCAI for ulcerative colitis (UC)), fortnightly health-related quality of life (HRQoL - derived from the EQ-5D-3L), and three-monthly healthcare use (ICHOM).

Aim: The aim of this study was to identify factors associated with hospitalisation, emergency department (ED) admission, and related costs using the longitudinal TC-IBD data.

Methods: Adults with IBD enrolled in TC-IBD (June 2018–Feb 2025) and ≥ 6 months of follow-up were included. Data were aggregated into 3-month panels using the most severe values within each period, and 3-month lagged variables to ensure temporal ordering. Random-effects logistic regression examined associations between HBI, SCCAI and EQ-5D scores, and subsequent hospitalisation or ED visits, adjusting for demographic and clinical covariates. An econometric panel-data random-effects model was used (in the fixed-effects/random-effects framework), partially accounting for unobserved heterogeneity. Annual costs were calculated using TC-IBD reported hospital use and unit costs, and population-level costs estimated by applying average per-patient event rates to the UK IBD population. Per patient event-rates of 2019 and 2020 were excluded to calculate the average per-patient event rates due to covid-19 bias. The assumed unit costs per hospitalisation and ED admission to calculate total related costs were £ 2976.59 and £ 241.99 respectively. An assumed UK IBD population of 500,000 patients was used to calculate estimated events and costs in the full UK IBD population. Analyses were performed in Stata 19.

Results: By Feb 2025, 3,197 patients were included (59.8% UC, 40.2% CD; median [IQR] age 45.5 [34.5–59.4] years and disease duration 4,000 [1,999–7,277] days), contributed 48,732 observations, with per patient a mean of 3.41 (SD 1.10) time periods per year and 15.2 in total. A total of 836 hospitalisations and 1,182 ED visits occurred among 501 and 672 patients respectively. Higher odds of hospitalisation and ED visits were associated with EQ-5D pain/discomfort (OR (95% CI) of 2.25 (1.57 - 3.22) with $p=0.000$ and 1.79 (1.31 - 2.43) with $p=0.000$ respectively) and limitations in usual activities (OR (95% CI) of 2.54 (1.74 - 3.72) with $p=0.000$ and 1.94 (1.42 - 2.66) with $p=0.000$ respectively), HBI general wellbeing (OR (95% CI) of 1.99 (1.61 - 2.47) with $p=0.000$ and 1.88 (1.58 - 2.24) with $p=0.000$ respectively) and HBI total score (OR (95% CI) of 1.19 (1.14 - 1.23) with $p=0.000$ and 1.16 (1.12 - 1.2) with $p=0.000$ respectively), SCCAI general wellbeing (OR (95% CI) of 1.62 (1.36 - 1.93) with $p=0.000$ and 1.99 (1.74 - 2.28) with $p=0.000$ respectively), SCCAI-reported blood in stool (OR (95% CI) of 1.31 (1.12 - 1.52) with $p=0.001$ and 1.18 (1.04 - 1.34) with $p=0.011$ respectively) and SCCAI total score (OR (95% CI) of 1.36 (1.29 - 1.43) with $p=0.000$ and 1.33 (1.27 - 1.38) with $p=0.000$ respectively). Decreased EQ-5D utility score was associated with increased ED use (OR (95% CI) of 0.31 (0.12 - 0.78) with $p=0.013$), while impaired self-care and overall health, higher HBI liquid stools and SCCAI bowel frequency were associated with hospitalisations (OR (95% CI) of 1.63 (1.04 - 2.57) with $p=0.035$; 0.98 (0.97 - 0.99) with $p=0.001$; 1.03 (1.01 - 1.05) with $p=0.006$ and 1.53 (1.23 - 1.89) with $p=0.000$). Yearly averages of 37,370 hospitalisations and 54,091 ED admissions were estimated for the full UK IBD population, with related average annual costs of £111,234,917 and £13,089,422 respectively.

Conclusions: This large longitudinal patient-reported dataset allowed to identify key factors - including general wellbeing and pain/discomfort in addition to total scores - associated with hospital and ED use, highlighting their potential for targeted real-time risk stratification, and enabled estimation of related costs. Findings on hospitalisations, ED admissions and related costs should be interpreted with caution due to the overlap with the covid-19 pandemic. Nonetheless, integrating remote monitoring into routine care may help enable proactive and cost-effective IBD management.

-I35-

LIPOPOLYSACCHARIDE-BINDING PROTEIN (LBP) AS A NOVEL NON-INVASIVE BIOMARKER OF DISEASE ACTIVITY IN INFLAMMATORY BOWEL DISEASE: INTERIM FINDINGS FROM THE PROBIO COHORT STUDY. L. Toris (1), C. Minsart (2), C. Husson (1), A. Cremer (3), L. Amininejad (3), D. Franchimont (2), C. Liefferinckx (2) / [1] ULB, Brussels, Belgium, Laboratory of Experimental Gastroenterology, [2] Hôpitaux Universitaires de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Belgium, Dept. Gastroenterology, Hepato-Pancreatology and Digestive Oncology, [3] HUB Hôpital Erasme, Brussels, Belgium, Dept. Gastroenterology, Hepato-Pancreatology and Digestive Oncology.

Introduction: Ileo-colonoscopy remains the gold standard for assessing Inflammatory Bowel Disease (IBD) activity, but its invasiveness and cost limit frequent use in clinical practice. Current biomarkers, including

C-reactive protein (CRP) and faecal calprotectin (FC), show suboptimal sensitivity and specificity, and FC adherence is often poor. Lipopolysaccharide-binding protein (LBP), a circulating acute-phase reactant binding bacterial lipopolysaccharides, reflects microbial translocation and intestinal permeability.

Aim: We aimed to evaluate LBP as a potential non-invasive biomarker of disease activity in IBD.

Methods: In this prospective observational study, adult patients (≥ 18 years) with established Crohn's disease (CD) or ulcerative colitis (UC) undergoing follow-up endoscopy were enrolled. Inclusion required endoscopic activity (SES-CD ≥ 4 for CD; Mayo ≥ 1 for UC). Exclusion criteria included chronic liver disease, pregnancy, proctocolectomy, or stoma. Study visits were scheduled at baseline, 8–16 weeks (V1), and 16–24 weeks (V2); only baseline and V1 data were considered for the present analysis. Clinical activity (PRO2), biomarkers (CRP, FC) and serum LBP were collected. Clinical response at V1 was defined using PRO2: CD non-response was $<50\%$ improvement; UC non-response was $<30\%$ improvement combined with <2 -point decrease and persistent rectal bleeding. All other patients were classified as responders. Diagnostic accuracy and associations between LBP, clinical indices and biomarkers were assessed using nonparametric tests and correlation analyses.

Results: Eighty-nine IBD patients were included (45 CD, 44 UC), of whom 53.9% were female. Median age was 40 years [IQR 30–54], and median BMI was 24.3 kg/m² [IQR 21.9–27.1]. According to Montreal classification, CD patients were distributed by age of diagnosis (A1 18%, A2 62%, A3 20%), disease behavior (B1 53%, B2 29%, B3 18%) and disease location (L1 35%, L2 27%, L3 38%, L4 27%). UC patients were categorized by disease extent as E1 16%, E2 41% and E3 43%. At baseline, 36% of the cohort exhibited mild (SES-CD = 4–10; Mayo = 1), 30.3% moderate (SES-CD = 11–20; Mayo = 2), and 33.7% severe (SES-CD >20 ; Mayo = 3) endoscopic activity. Almost two thirds of the IBD cohort (65.2%) were treated by biologics and 15.7% by immunosuppressors. In addition, 30.3% of patients used topical or systemic steroids. Baseline biomarker levels were as follows: median CRP was 14.1 mg/L [IQR 3.7–26.4] in CD and 2.8 mg/L [IQR 1.6–5.5] in UC; median FC was 464 $\mu\text{g/g}$ [IQR 167–1602] in CD and 205 $\mu\text{g/g}$ [IQR 88–1394] in UC. Median serum LBP concentrations reached 7717 ng/mL [IQR 6179–9734] in CD and 6430 ng/mL [IQR 4731–8639] in UC ($p < 0.1$). At baseline, LBP correlated strongly with CRP ($\rho = 0.546$, $p < 0.001$) and moderately with endoscopic activity ($\rho = 0.31$, $p < 0.01$), but not with FC. When excluding corticosteroid-treated patients who displayed normal CRP values, the LBP-CRP correlation increased further ($\rho = 0.594$, $p < 0.001$), suggesting that LBP levels remain unaffected by corticosteroid therapy. Consistently, LBP also correlated positively with PRO2 scores ($\rho = 0.293$, $p < 0.01$), supporting its association with both objective biomarkers and patient-reported disease activity. Between baseline and V1, changes in LBP (ΔLBP) positively correlated with changes in CRP (ΔCRP) ($\rho = 0.455$, $p < 0.01$), supporting the value of LBP in capturing dynamic inflammatory responses. Notably, clinical non-responders exhibited a significant increase in LBP from baseline to Visit 1 ($p < 0.05$), suggesting that LBP may serve as an early marker of clinical response.

Conclusions: In this interim analysis of the prospective PROBIO cohort of active IBD, serum LBP demonstrated strong correlation with objective inflammatory markers (CRP, endoscopy) and patient-reported outcomes, while remaining unaffected by corticosteroids. LBP further captured longitudinal changes in systemic inflammation and increased among clinical non-responders. These findings support LBP as a promising novel non-invasive biomarker for disease activity and treatment monitoring in IBD.

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EFFICACY AND SAFETY OF OBEFAZIMOD IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: RESULTS FROM TWO, PHASE 3, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, 8-WEEK INDUCTION TRIALS (ABTECT-1 & 2). F. Baert (1), N. Deprez (2), J. Rahier (3), V. Muls (4), T. Lobatón Ortega (5), D. Franchimont (6), B. Verstockt (7), G. D'Haens (8), F. Cataldi (9), D. Jacobstein (10), C. Rabbat (9), S. Kevin (11), S. Vermeire (12) / [1] AZ Delta, Belgium, Gastroenterology, [2] AZ Maria Middelaes, Ghent, Belgium, Gastroenterology, [3] CHU UCL Namur, Yvoir, Belgium, Gastroenterology, [4] CHU Saint-Pierre, Brussels, Belgium, Gastroenterology, [5] University Hospital of Ghent, Belgium, Internal Medicine and Paediatrics - Gastroenterology, [6] Erasmus University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology, [7] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology & Hepatology, [8] Amsterdam University Medical Centres, Amsterdam, The Netherlands, Gastroenterology & Hepatology, [9] Abivax, Paris, France, Medical Affairs, [10] Abivax, Paris, France, Clinical Development, [11] Abivax, Paris, France, Biometrics, [12] KU Leuven, Leuven, Belgium, Gastroenterology & Hepatology.

Introduction: Obefazimod (Obe) is an oral, once-daily (QD), small molecule which enhances

expression of microRNA-124 and has been studied in two Phase 2 induction trials and subsequent open-label maintenance studies in patients (pts) with moderately to severely active ulcerative colitis (UC). **Aim:** Here we report efficacy and safety of two Phase 3, 8-week, induction trials in adult pts with UC from ABTECT-1 [NCT05507203] and ABTECT-2 [NCT05507216].

Methods: The multicentre, randomized, double-blind, placebo-controlled ABTECT trials enrolled pts with moderate-to-severe UC (defined as modified Mayo score (MMS) ≥ 5 , with rectal bleeding sub-score (RBS) ≥ 1 and centrally read endoscopic score >2) who had inadequate response, loss of response, or intolerance to at least one prior therapy (with no upper limit), including corticosteroids, immunosuppressants, biologics, S1P receptor modulators and/or JAK inhibitors. Pts were randomized 2:1:1 to Obe 50 mg QD (Obe-50), Obe 25 mg QD (Obe-25) or placebo (PBO) for 8 weeks. The primary endpoint was clinical remission (stool frequency sub-score (SFS) ≤ 1 , RBS = 0 and endoscopic sub-score (ES) ≤ 1) and secondary endpoints included clinical response (decrease from baseline in the MMS ≥ 2 points and $\geq 30\%$ from baseline, plus a decrease in RBS ≥ 1 or an absolute RBS ≤ 1), endoscopic improvement (ES ≤ 1), symptomatic remission (RBS=0, SFS <1), and histo-endoscopic mucosal improvement (HEMI, Geboes histologic score ≤ 3.1 and ES ≤ 1). Non-responder imputation (NRI) was used for pts with missing outcome at Week 8. % Difference was for Obe minus PBO and was based on estimated common risk difference using the Mantel-Haenszel weights adjusting for the randomization stratification factors (inadequate response to advanced therapies (yes/no), baseline oral corticosteroids usage (yes/no), and region (Japan/rest of world) [ABTECT-2 only]. P-values were two sided; for pooled analysis, all p-values were nominal.

Results: 1272 pts were randomized and treated in ABTECT-1 (636) and ABTECT-2 (636). In both trials, baseline demographics and disease characteristics were similar between groups; 45.3% and 49.3% of pts had inadequate response to 1 or more advanced therapies. A significantly higher proportion of pts receiving Obe-50 (ABTECT-1: 21.7%, ABTECT-2: 19.8%) versus PBO (2.5% and 6.3%) achieved clinical remission (Obe-50-PBO difference: ABTECT-1: 19.3%, $p < 0.0001$; ABTECT-2: 13.4%, $p = 0.0001$) and met all key secondary endpoints in both trials. A significantly higher proportion of pts receiving Obe-25 (23.8%) versus PBO (2.5%) achieved clinical remission (Obe-25-PBO difference: 21.4%, $p < 0.0001$) and met all key secondary endpoints in ABTECT-1. In a pooled analysis, both Obe-50 and Obe-25 met all primary and secondary endpoints with nominal significance (clinical remission - Obe-25-PBO difference: 13.2%, $p < 0.0001$, Obe-50-PBO difference: 16.4%, $p < 0.0001$; clinical response - Obe-25-PBO difference: 28.6%, $p < 0.0001$, Obe-50-PBO difference: 31.2%, $p < 0.0001$; endoscopic improvement - Obe-25-PBO difference: 21.9%, $p < 0.0001$, Obe-50-PBO difference: 26.6%, $p < 0.0001$; HEMI - Obe-25-PBO difference: 13.2%, $p < 0.0001$, Obe-50-PBO difference: 18.2%, $p < 0.0001$; symptomatic remission - Obe-25-PBO difference: 18.1%, $p < 0.0001$, Obe-50-PBO difference: 21.0%, $p < 0.0001$). The overall rate of serious adverse events and treatment emergent adverse events (TEAEs) leading to study drug discontinuation for pts treated with Obe were similar to PBO. Proportions of pts who reported at least one TEAE in ABTECT-1 were 59.4%, 46.9%, and 53.2% for Obe-50, Obe-25, and PBO, respectively. For ABTECT2, TEAEs occurred in 61.0%, 50.9%, and 48.4% for Obe-50, Obe-25, and PBO, respectively. The most frequent TEAE was headache (Obe-50: 20.8-25.8%; Obe-25: 14.5-15.6%; PBO: 5.7). The headaches were mild, transient, short in duration and not a barrier to treat as evidenced by a low discontinuation rate of 0-1.6%. No signal was observed for serious, severe, or opportunistic infections or malignancies.

Conclusions: In both ABTECT induction trials, primary and secondary endpoints were met; obe treatment led to statistically significant improvements in clinical, endoscopic, symptomatic and combined endoscopic-histologic endpoints at week 8. Obe was well tolerated with no new safety signals identified.

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SHARED PATHWAYS, UNEQUAL ENGAGEMENT: SKIN TRANSCRIPTOMICS DISTINGUISH PARADOXICAL ANTI-TNF INDUCED FROM CONVENTIONAL PSORIASIS IN IBD. A. D'Hooghe (1), T. Hillary (2), A. Moens (3), S. Verstockt (4), S. Abdurahiman (4), J. Sabino (3), K. Van Hoeve (5), S. Vermeire (4), M. Ferrante (3), B. Verstockt (3) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology, [2] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Dermatology, [3] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Gastroenterology and Hepatology, [4] KU Leuven, Leuven, Belgium, Translational Research Centre for Gastrointestinal Disorders (TARGID), [5] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Paediatric gastroenterology & Hepatology & Nutrition.

Introduction: Anti-tumour necrosis factor (anti-TNF) therapy is widely used as first-line treatment

for inflammatory bowel diseases (IBD). Although generally safe, ~6% of patients develop paradoxical psoriasiform lesions (PP), sometimes necessitating therapy withdrawal. The underlying mechanisms remain unclear.

Aim: In this study, we compared the transcriptomic landscapes of PP and conventional psoriasis (PsO) to characterize both convergent and divergent molecular pathways contributing to their clinically similar presentations.

Methods: Paired lesional and non-lesional skin punch biopsies were obtained from 7 IBD patients with anti-TNF-induced PP, alongside 10 PsO lesional biopsies. RNA-seq (Illumina TruSeq) was performed, complemented by public datasets from 9 healthy controls (HC) and 10 PsO lesions. Weighted gene co-expression network analysis (WGCNA) defined modules associated with PP and PsO. Significant modules were defined as having a false discovery rate corrected p-value (p_{adj}) of less than 0.05. Top enriched pathways and upstream regulators were analysed with ingenuity pathway analysis and gene set enrichment analysis.

Results: WGCNA identified 26 co-expression modules, three of which showed significant associations with both lesional PP and PsO: M1 (upregulated), M2 (upregulated), and M3 (downregulated), with correlations generally stronger in PsO. M1 (PP: correlation $[r]=0.85$, $p_{adj}=9 \times 10^{-4}$; PsO: $r=0.84$, $p_{adj}=1 \times 10^{-6}$) was enriched for innate immune response (neutrophil degranulation, IFN α/β and IFN γ signalling), with TNF, IFN α and IFN γ as major predicted upstream regulators. M2 (PP: $r=0.69$, $p_{adj}=0.05$; PsO: $r=0.78$, $p_{adj}=3 \times 10^{-5}$) highlighted enhanced proliferation programmes (mitotic and cell-cycle processes), compatible with keratinocyte hyperproliferation. M3 (PP: $r=-0.78$, $p_{adj}=0.01$, PsO: $r=-0.88$, $p_{adj}=7 \times 10^{-8}$) was downregulated in both PP and PsO, enriched for generic transcription pathway, with key hub genes functioning in Notch, Wnt, and NF- κ B signalling, suggesting reduced regulatory control. A single PsO-specific module (M4), enriched for NF1 RAS signaling and extracellular matrix organization, was uniquely downregulated in PsO ($r=-0.58$, $p_{adj}=0.03$), pointing again to a loss of epidermal differentiation cues and impaired tissue integrity.

Conclusions: PP and PsO share key inflammatory, proliferative, and differentiation-related pathways. The proliferative pathways are more significantly activated in PsO as compared to PP, while the upregulation of innate immune response pathways is comparable.

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EARLYDISEASEACTIVITYINFORMSREAL-WORLDRESPONSETOETRASIMODINULCERATIVE COLITIS. L. Derluyn (1), M. Ferrante (2), J. Sabino (2), B. Verstockt (2) / [1] KUL - University of Leuven, Leuven, Belgium, Translational Research in Gastrointestinal Disorders (TARGID), Department of Chronic Diseases and Metabolism (CHROMETA), [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Etrasimod is an oral S1P-receptor modulator for ulcerative colitis (UC), demonstrating ~25 % clinical remission at week 12 in ELEVATE. In the recent GLADIATOR study, remission at week 12 was observed ~28% of more mild UC patients.

Aim: Real-world evidence remains scarce, motivating this study.

Methods: Adults with active UC (endoscopic Mayo sub-score, EMS ≥ 2) initiating etrasimod 2mg daily between October 2024 and August 2025 were prospectively monitored. Patients with an ostomy or an IPAA were excluded. Clinical assessments were performed at week (w)4, w8 and month 6; endoscopy was repeated at w8. Symptomatic remission was defined as a partial modified Mayo score ≤ 1 (stool frequency sub-score of 0 [or stool frequency of 1 with a ≥ 1 -point decrease from baseline] and rectal bleeding 0). Symptomatic response was defined as a decrease in partial modified Mayo score of 30%. Endoscopic improvement and remission were defined as an Mayo endoscopic sub-score of 0, or ≤ 1 respectively. Non-responder imputation and last observation carried forward analysis were applied. Time-to-discontinuation to month 6 was analysed using Kaplan–Meier and log-rank tests comparing baseline moderate–severe (Modified Mayo score, MMS > 6) vs mild–moderate disease (MMS ≤ 6).

Results: Twenty patients were included. Median follow-up was 27.1 [24.0–46.2] weeks, with median exposure of 24.4 [17.4–35.4] weeks. Partial modified Mayo improved from 3.0 [2.0–4.3] at baseline to 2.0 [0.8–3.0] at w4 ($p=0.007$), with 45% and 20% of patients achieving, respectively, symptomatic response, remission. By w8, scores decreased to 1.0 [0.0–3.0] ($p=0.006$), with 45% of patients achieving (steroid-free) symptomatic remission. Endoscopic improvement and remission at w8 were observed in, respectively, 50% and 20% of patients. All w8 symptomatic remitters remained in steroid-free (i.e. at day of assessment) symptomatic remission through month 6. At w4, pMMS predicted outcomes: each 1-point increase reduced

odds of symptomatic remission at w8 (OR 0.21 [95% CI 0.05–0.82]; $p=0.03$), endoscopic response at w8 (0.41 [0.18–0.96]; $p=0.04$), and symptomatic remission at month 6 (0.15 [0.03–0.89]; $p=0.04$). A higher w4 white blood cell count predicted lower likelihood of symptomatic remission at month 6 (per $1 \times 10^9/L$ 0.38 [0.14–1.00]; $p=0.049$). Overall, 30% of patients discontinued etrasimod after a median of 12.0 [10.5–11.0] weeks, mainly due PNR ($n=3$). Discontinuation was more common in moderate-to-severe disease (42.9% vs 7.7%; $p=0.10$). Kaplan–Meier analysis showed shorter time-to-discontinuation in this group ($p=0.03$). No new safety concerns emerged.

Conclusions: Etrasimod induced rapid symptomatic and endoscopic improvements with meaningful w8 remission and sustained steroid-free symptomatic remission to month 6. Early on, treatment disease activity, particularly w4 partial modified Mayo and WBC count, was prognostic. Discontinuation was more frequent in patients with moderate–severe UC. These real-world findings support etrasimod as an effective and well-tolerated therapy in routine clinical practice.

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EVALUATION OF MULTIDISCIPLINARY MANAGEMENT OF PATIENTS WITH IBD AND CONCURRENT EXTRA-INTESTINAL MANIFESTATIONS AND IMMUNE-MEDIATED INFLAMMATORY DISORDERS: A RETROSPECTIVE STUDY. M. Truyens (1), X. Tolstoy (2), G. Calabrese (3), P. Balestrieri (4), K. Argyriou (5), A. Blesl (6), L. Pouillon (7), E. Shakweh (8), R. Filip (9), I. Drygiannakis (10), A. Todeschini (11), G. Mocci (12), P. Ploutarchos (13), D. Ribaldone (14), A. Jauregui-Amezaga (15), I. Yudego (16), S. Vieujean (17), K. Karmiris (18), T. Taelman (19), H. Kani (20), M. García (21), A. Cremer (22), E. Savarino (23), C. Felice (24), H. Gordon (25), N. Vladimirova (26), M. Attaubi (27), M. Barreiro de Acosta (28), H. Peeters (29), M. Georgios (30), T. Innocenti (31), T. Holvoet (32), A. Gutiérrez (33), M. Estevinho (34), T. Karakan (35), S. Vrakas (36), M. Casanova (37), C. Kapizioni (38), N. Noor (39), G. Dagci (40), J. Geldof (41), O. Nardone (42), I. Koutroubakis (10), G. Varkas (43), J. Lambert (44), T. Lobatón Ortega (41) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology, [2] Karolinska Institutet, Karolinska University Hospital, Sweden, Department of Gastroenterology, Dermatovenereology and Rheumatology, [3] University of Naples Federico II, Naples, Italy, Department of Clinical Medicine and Surgery, [4] Fondazione Campus Bio-Medico, Rome, Italy, Gastroenterology Unit, [5] General University Hospital of Larissa, Greece, Larissa, Greece, Department of Gastroenterology, [6] Medical University of Graz, Graz, Austria, Department of Internal Medicine, [7] Imelda General Hospital, Belgium, Department of Gastroenterology and Hepatology, [8] St Mark's National Bowel Hospital, United Kingdom, London Department of Metabolism, Digestion and Reproduction, [9] University of Rzeszow, Rzeszów, Poland, Department of Internal Medicine, Faculty of Medicine, Collegium Medicum, [10] University Hospital of Heraklion, Crete, Greece, Department of Gastroenterology, [11] IRCCS Sacro Cuore Don Calabria Hospital Negrar di Valpolicella, Verona, Italy, IBD unit, [12] Brotzu Hospital, Cagliari, Italy, Division of Gastroenterology, [13] University of Patras, Patras, Greece, Department of Internal Medicine, [14] University of Turin, Italy, Department of Medical Sciences, [15] Antwerp University Hospital, Edegem, Belgium, Department of Gastroenterology and Hepatology, [16] Hospital Universitario de Galdakao- Biobizkaia Health Research Institute, Spain, Servicio de Aparato Digestivo, [17] Clinique Saint-luc Bouge, Namur, Belgium, Hepato-gastroenterology Department, [18] Venizeleio General Hospital, Heraklion, Crete, Greece, Department of Gastroenterology, [19] AZ Groeninge, Kortrijk, Belgium, Department of Gastroenterology, [20] Marmara University Faculty of Medicine, Istanbul, Turkey, Department of Gastroenterology, [21] Universidad de Cantabria, Santander (Cantabria), Spain, Gastroenterology and Hepatology Department, [22] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Gastroenterology, [23] University of Padua, Padua, Italy, Gastroenterology Unit, [24] University Hospital Treviso, Treviso, Italy, Medicine 1 Unit, [25] Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom, Translational Gastroenterology Unit, [26] Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark, Copenhagen Centre for Arthritis Research, [27] Copenhagen University Hospital - Amager and Hvidovre, Denmark, Department of Gastroenterology and Hepatology, [28] Hospital Clínico Universitario de Santiago de Compostela, Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain, Department of gastroenterology, [29] AZ Sint-Lucas Gent, 9000, Belgium, Department of gastroenterology, [30] General Hospital of Athens 'G. Gennimatas', Athens, Greece, Department of gastroenterology, [31] Careggi University Hospital, Florence, Italy, IBD Referral Centre, Clinical Gastroenterology Unit, [32] VITAZ, Sint-Niklaas, Belgium, Department of Gastroenterology, [33] Alicante General University Hospital, Alicante, Spain, Department of Gastroenterology, [34] Unidade Local de Saúde Gaia Espinho, Vila Nova de Gaia, Portugal, Department of Gastroenterology, [35] Gazi University,

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Introduction: Extra-intestinal manifestations (EIMs) and co-existing immune-mediated inflammatory diseases (IMIDs) are common in patients with inflammatory bowel disease (IBD) and may influence treatment decisions and outcomes. Optimal management often requires collaboration between gastroenterologists, dermatologists and rheumatologists. However, how such multidisciplinary care is organised in daily practice across centres and countries remains insufficiently characterised.

Aim: The aim of this study was to describe how multidisciplinary care is organised across centres and to assess the extent to which patients with EIMs/IMIDs were evaluated by the appropriate specialist (dermatologist or rheumatologist). This analysis was conducted as a substudy within the ECCO National Study Group project "Assessing the effect of newer treatment molecules for IBD on extra-intestinal manifestations and concurrent immune-mediated inflammatory diseases (IMPACT-IBD)".

Methods: IMPACT-IBD was a retrospective, international, multicentric study evaluating the response of EIMs/IMIDs in patients with IBD treated with JAK inhibitors or selective IL-23 inhibitors. Patients with ulcerative colitis or Crohn's disease who had at least one dermatological or rheumatological EIM/IMID at baseline and who initiated treatment with a JAK inhibitor or an IL-23 inhibitor were eligible for inclusion. Dermatological manifestations comprised psoriasis, hidradenitis suppurativa, erythema nodosum and pyoderma gangrenosum, while rheumatological manifestations included axial and/or peripheral spondyloarthritis (including psoriatic arthritis). This substudy specifically assessed: (1) how multidisciplinary IMID meetings were organised across participating centres; (2) the proportion of patients who were evaluated by the appropriate specialist (dermatologist and/or rheumatologist) at each study timepoint (baseline, post-induction, month 6 and month 12 after treatment initiation); and (3) the proportion of EIM/IMID cases that were discussed during these multidisciplinary IMID meetings.

Results: A total of 297 IBD patients from 39 centres across 11 countries were included. Twenty-four centres reported organising a multidisciplinary IMID meeting. The presence of such meetings varied across countries: Belgium (5/8 centres), Austria (1/1), Turkey (2/3), the United Kingdom (0/2), Italy (4/8), Spain (5/5), Portugal (1/1), Greece (4/7), Denmark (1/2), Sweden (1/1) and Poland (0/1). At baseline, 117/280 patients had a dermatological EIM/IMID, including psoriasis (n=71), hidradenitis suppurativa (n=23), erythema nodosum (n=20) and/or pyoderma gangrenosum (n=13; multiple conditions possible). At treatment initiation a dermatologist assessed 59/117 patients (50.4%), significantly more frequently in centres with an IMID meeting compared with those without (40/65 (61.5%) vs 19/52 (36.5%); $P=0.007$). Post-induction, 26/106 patients (24.5%) were reviewed by a dermatologist, again predominantly in centres with a multidisciplinary meeting (21/62 (33.9%) vs 5/44 (11.4%); $P=0.008$). By month 6, dermatological evaluation was limited to 19/77 patients (24.7%), but remained more common in IMID-meeting centres (17/53 (32.1%) vs 2/24 (8.3%); $P=0.025$). At month 12, assessment decreased further to 7/49 patients (14.3%), with no significant difference between centres with and without IMID meetings (5/30 (16.7%) vs 2/19 (10.5%); $P=0.550$). Over the entire follow-up, 46/117 patients (39.3%) with dermatological EIMs/IMIDs were ever discussed in an IMID meeting. Rheumatological EIMs/IMIDs were present in 200/282 patients, including axial spondyloarthritis (n=116) and/or peripheral spondyloarthritis (n=123). At baseline, 163/200 patients (81.5%) were assessed by a rheumatologist, with numerically higher involvement in IMID-meeting centres (109/128 (85.2%) vs 54/72 (75.0%); $P=0.076$). Post-induction, rheumatology evaluation occurred in 86/180 patients (47.8%), again more frequently in centres with an IMID meeting (62/115 (53.9%) vs 24/65 (36.9%); $P=0.028$). At month 6, rheumatological assessment was performed in 64/143 patients (44.8%), with numerically higher rates in centres with a multidisciplinary meeting (48/96 (50%) vs 16/47 (34%); $P=0.071$). By month 12, 43/91 patients (47.3%) underwent rheumatological evaluation, without statistically significant differences between IMID-meeting and non-meeting centres (30/60 (50%) vs 13/31 (41.9%); $P=0.465$). Across the cohort, 88/200 patients (44.0%) with rheumatological EIMs/IMIDs were ever discussed in an IMID meeting.

Conclusions: This international multicentric study demonstrates variation in how IMID- and EIM-related care for IBD is organised across centres and countries. Despite the presence of multidisciplinary

structures in many centres, specialist involvement was inconsistent over time. These exploratory findings highlight opportunities to optimise multidisciplinary pathways for patients with EIMs/IMIDs. Further research is required to evaluate whether such coordinated approaches lead to better patient outcomes.

-I40-

THE PSYCHOLOGICAL BURDEN OF INFLAMMATORY BOWEL DISEASE: A GLOBAL SURVEY ASSESSING THE ROLE OF REGION, AGE AND SEX. M. Vanhaverbeke (1), L. Fierens (1), M. Walentynowicz (2), J. Horrigan (3), B. Keersmaekers (4), J. Salwen-Deremer (3), I. Van Diest (5), C. Siegel (3), A. Hart (6), M. Ferrante (4) / [1] Translational Research Centre for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism (CHROMETA), [2] University of Southern California, Los Angeles, United States, Centre for Self-Report Science and Centre for Economic & Social Research, [3] Dartmouth Hitchcock Medical Centre, Lebanon, United States, Centre for Digestive Health, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [5] KU Leuven, Leuven, Belgium, Research Group Health Psychology, [6] St Mark's National Bowel Hospital, United Kingdom, IBD Unit.

Introduction: Inflammatory bowel diseases (IBD) can significantly affect patients' mental well-being and overall quality of life (Lönnfors S et al. J Crohns Colitis. 2014). Consequently, monitoring both functional and psychological aspects is essential to comprehensively assess the disease burden and enhance patient outcomes (Williet N et al. Clinical Gastroenterology and Hepatology. 2014).

Aim: This study aimed to examine psychological burden of IBD in a global cohort and to explore potential differences across regions, age groups and sex.

Methods: A list of 72 items, categorized into 5 domains was developed based on existing quality of life questionnaires assessing the burden of IBD. Patients (≥ 18 y/o) from Europe, North America and Oceania were recruited through social platforms and patient organizations. They were requested to rate each item on a 9-point rating scale (1 – 3 = yearly or almost yearly, 7 – 9 = weekly to daily) in response to the question: Due to your IBD, how frequently have you experienced this item over the course of your life with IBD'. This study focuses specifically on the scoring of the 16 items within the domain psychological burden in relation to patients' age, region and gender.

Results: Between August 18th and October 22nd 2025, 408 out of the 508 responding patients completed the survey. This final cohort consisted of 277 (67.9%) European, 101 (90.4%) North-American and 30 (7.4%) Oceanian patients. More women ($n = 301$, 73.8%) than men ($n = 107$, 26.2%) completed the survey. There was an almost equal representation of patients with Crohn's disease ($n = 213$, 52.2%) and ulcerative colitis ($n = 190$, 46.6%), with a small group diagnosed with IBD type unclassified ($n = 5$, 1.2%). The participants were predominantly 35 – 49 years old ($n = 149$, 36.5%), followed by those aged 18 – 34 years ($n = 121$, 29.7%), 50 – 64 years ($n = 92$, 22.5%), and ≥ 65 years ($n = 46$, 11.3%). Responder analysis showed that patients without prior participation in a survey study were less likely ($p=0.018$), and those who had undergone surgery more likely ($p=0.029$) to complete the survey. Pairwise ANCOVA analyses corrected for multiple testing showed that feelings of tearfulness, sadness or being upset were reported more frequently by participants from Europe vs North America ($p = 0.01$). These feelings ($p = 0.029$), as well as embarrassment ($p = 0.004$), stress or tension ($p = 0.029$), guilt ($p = 0.020$), negative body image ($p = 0.001$), fatigue ($p = 0.016$), difficulties accepting the disease ($p = 0.006$), and challenges in performing household tasks ($p = 0.028$) were reported more frequently by women than men. Women also reported a frequenter decrease in general well-being overall ($p = 0.019$). This pattern of higher frequency of psychological burden among women was also reflected in age-related differences. Participants aged 18 – 34 years more often experienced unhappiness and dissatisfaction with their personal life ($p = 0.026$), fear of needing surgery ($p = 0.027$) and fatigue ($p = 0.004$) compared with those aged 50 – 64 years old. Compared with the same reference group, participants aged 18 – 49 years reported more difficulties accepting the disease ($p = 0.015$), feeling less attractive ($p = 0.017$) and social isolation ($p = 0.001$). Fear of cancer was also more common in participants aged 18 – 34 years old ($p = 0.015$) and 35 – 49 years old ($p = 0.001$). Finally, fear of stigmatization ($p = 0.014$) and the need to justify their disease in social contexts ($p = 0.017$) were more frequently reported in those aged 35 – 49 years than in those aged 50 – 64 years.

Conclusions: Psychological burden trends were mostly the same across Europe, North America and Oceania. However, results showed that women and younger patients reported a higher frequency of psychological burden. Findings highlight the need for a holistic approach that addresses both clinical symptoms and mental health to improve the overall quality of life for patients with IBD.

EFFICACY OF OBEFAZIMOD IN ABTECT PHASE 3 INDUCTION TRIALS: RESULTS OF 8-WEEK THERAPY IN SUBSETS OF PATIENTS WITH AND WITHOUT PRIOR INADEQUATE RESPONSE TO ADVANCED THERAPIES. F. Baert (1), N. Deprez (2), J. Rahier (3), V. Muls (4), T. Lobatón Ortega (5), D. Franchimont (6), B. Verstockt (7), G. D'Haens (8), F. Cataldi (9), D. Jacobstein (10), C. Rabbat (9), K. Shan (11), S. Vermeire (12) / [1] AZ Delta, Belgium, Gastroenterology, [2] AZ Maria Middelaers, Ghent, Belgium, Gastroenterology, [3] CHU UCL Namur, Yvoir, Belgium, Gastroenterology, [4] CHU Saint-Pierre, Brussels, Belgium, Gastroenterology, [5] University Hospital of Ghent, Belgium, Internal Medicine and Paediatrics - Gastroenterology, [6] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology, [7] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [8] Amsterdam University Medical Centres, Amsterdam, The Netherlands, Gastroenterology, [9] Abivax, Paris, France, Medical Affairs, [10] Abivax, Paris, France, Clinical Development, [11] Abivax, Paris, France, Biometrics, [12] KU Leuven, Leuven, Belgium, Gastroenterology.

Introduction: Obefazimod (Obe), an oral, once-daily (QD), small molecule which enhances expression of microRNA-124 was studied in patients (pts) with moderately to severely active ulcerative colitis (UC) in Phase 2 studies.

Aim: Here we present efficacy endpoints at week 8 for pts with and without prior inadequate response to advanced therapies (AT-IR-Yes, AT-IR-No) from ABTECT-1 [NCT05507203] and ABTECT-2 [NCT05507216] Phase 3 trials.

Methods: The multicentre, randomized, double-blind, placebo-controlled ABTECT trials enrolled pts with moderate-to-severe UC (modified Mayo score, MMS ≥ 5 , with rectal bleeding sub-score (RBS) ≥ 1 and centrally read endoscopic score >2) who had inadequate response, loss of response, or intolerance to at least one prior therapy (with no upper limit), including corticosteroids, immunosuppressants, biologics, S1P receptor modulators and/or JAK inhibitors (JAKi). Pts were randomized 2:1:1 to Obe 50 mg QD (Obe-50), Obe 25 mg QD (Obe-25) or placebo (PBO) for 8 weeks. Clinical remission per MMS (stool frequency sub-score (SFS) ≤ 1 , RBS = 0 and endoscopic sub-score (ES) ≤ 1), clinical response (decrease from baseline in the MMS ≥ 2 points and $\geq 30\%$ from baseline, plus a decrease in RBS ≥ 1 or an absolute RBS ≤ 1), endoscopic improvement (ES ≤ 1), symptomatic remission (RBS=0, SFS <1), and histo-endoscopic mucosal improvement (HEMI, Geboes histologic score ≤ 3.1 and ES ≤ 1) were analysed among AT-IR-Yes and AT-IR-No pts; all p-values are nominal.

Results: Among pts who participated in ABTECT-1, ABTECT-2, and the pooled analysis, 45.3% (288/636), 49.4% (314/636), and 47.3% (602/1272) were AT-IR-Yes, respectively; 54.7% (348/636), 50.6% (322/636), 52.7% (670/1272) were AT-IR-No. In ABTECT-1, ABTECT-2, and pooled, a higher proportion of the AT-IR-Yes subgroup receiving Obe-50 achieved clinical remission relative to PBO (Obe-50-PBO difference: ABTECT-1 12.7%, $p=0.0039$; ABTECT-2 7.6%, $p=0.0652$, pooled 10.1%, $p=0.0009$), clinical response (Obe-50-PBO difference: ABTECT-1 32.5%, $p<0.0001$; ABTECT-2 36.8%, $p<0.0001$, pooled 34.9%, $p<0.0001$), endoscopic improvement (Obe-50-PBO difference: ABTECT-1 17.8%, $p=0.0011$; ABTECT-2 17.7%, $p=0.0015$, pooled 17.8%, $p<0.0001$), HEMI (Obe-50-PBO difference: ABTECT-1 11.3%, $p=0.0073$; ABTECT-2 11.0%, $p=0.0197$, pooled 11.1%, $p=0.0005$), and symptomatic remission (Obe-50-PBO difference: ABTECT-1 25.0%, $p=0.0001$; ABTECT-2 21.7%, $p=0.0006$, pooled 23.4%, $p<0.0001$). In the AT-IR-Yes subgroup, the difference from PBO across all efficacy measures was lower for pts receiving Obe-25 relative to Obe-50. In the AT-IR-No subgroup, larger proportions achieved all efficacy measures relative to PBO including clinical remission (Obe-50-PBO difference: ABTECT-1 25.0%, $p<0.0001$; ABTECT-2 19.4%, $p=0.0004$; pooled 22.4%, $p<0.0001$ - Obe-25-PBO difference: ABTECT-1 32.4%, $p<0.0001$; ABTECT-2 9.5%, $p=0.0659$; pooled 21.3%, $p<0.0001$). In the AT-IR-No subgroup, Obe-50 and Obe-25 performed similarly in the pooled analysis across efficacy measures. In the subset of pts who failed JAKi, higher proportion of pts receiving Obe-50 or Obe-25 achieved clinical response relative to PBO (Obe-50-PBO difference, pooled 34.4%, $p=0.0017$; Obe-25-PBO difference, pooled 27.0%, $p=0.0196$). The difference from PBO in clinical response for Obe-25 and Obe-50 was similar across lines of treatment, from AT-IR-No through 4+ AT-IRs. Obefazimod was well tolerated with a safety profile similar to previous studies.

Conclusions: Among AT-IR-Yes and AT-IR-No subgroups, improvements in clinical, endoscopic, symptomatic and combined endoscopic-histologic measures were observed in pts treated with Obe at week 8 relative to PBO in ABTECT-1, ABTECT-2, and in the pooled analysis. Improvements vs. PBO in clinical response were observed in a pooled analysis in AT-IR-Yes JAKi-IR pts and across lines of therapy up to 4+ AT-IR.

INNOVATIVE IN SITU 4D BIOPRINTING FOR REGENERATION OF COLORECTAL MUCOSA AND SUBMUCOSA. T. Benoot (1), R. Santos Silva (2), J. Groll (3), T. Juengst (3), A. Ewald (3), G. Vozzi (4), I. Chiesa (4), A. Arezzo (5), F. Barontini (5), C. Brovarone (6), A. Bal-Öztürk (7), A. Bernkop-Schnurch (8), I. Vicini (9), S. Van Vlierberghe (10), D. Laukens (11) / [1] Ghent University, Ghent, Belgium, Internal Medicine and Paediatrics, [2] Ghent University, Ghent, Belgium, Department of Organic and Macromolecular Chemistry, [3] University of Würzburg, Würzburg, Germany, Department of Functional Materials in Medicine and Dentistry, [4] University of Pisa, Pisa, Italy, Department of Bioengineering and Robotics Research, [5] University of Torino, Torino, Italy, Department of Surgical Sciences, [6] Polytechnic University of Turin, Torino, Italy, Department of Applied Science and Technology, [7] AdBioInk Biosystem Technology, Kocaeli, Turkey, AdBioInk Biosystem Technology, [8] Thiomatrix, Innsbruck, Austria, Department of R&D, Thiomatrix, [9] Bewarrant, Brussels, Belgium, Department of European Funding Development, [10] Ghent University, Ghent, Belgium, Department of Organic and Macromolecular Chemistry, [11] Ghent University, Ghent, Belgium, Department of Internal Medicine and Paediatrics.

Introduction: Familial adenomatous polyposis and ulcerative colitis severely impact patients' daily functioning and overall well-being. No curative therapy currently exists, and patients often require proctocolectomy followed by ileal pouch construction. While continence is preserved, this procedure carries significant complications and may sometimes necessitate conversion to a terminal ileostomy. The EU-funded project TENTACLE aims to develop an innovative in situ 4D bioprinting system to fabricate shape-morphing, layered bioconstructs laden with primary cells (fibroblasts and epithelial cells) directly on the patient's decellularized rectal tissue (Fig. 1). These bioconstructs, composed of thiolated polysaccharides and/or thiol-ene photo-crosslinkable gelatin-based matrices, will permit controlled release of antibiotics and antifibrotics to promote cellular repopulation of the rectum.

Aim: The aim is to establish the design and formulation of the thiol-ene photo-crosslinked gelatin hydrogel composed of a mixture between gel-norbornene (GelNB) and thiolated gel (GelSH). Specifically, we seek to identify the optimal composition of the norbornene- and thiol-modified gelatin to generate a hydrogel network suitable for intestinal fibroblast encapsulation.

Methods: GelNB was developed by converting the carboxylic acid functionalities in 5-norbornene-2-carboxylic acid into an activated succinimide ester via reaction with N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (EDC) and N-Hydroxysuccinimide (NHS), achieving a 90% degree of substitution. Removal of residual EDC, NHS and norbornene through precipitation with acetone followed by 24h dialysis at 40°C was essential to prevent undesired zero-length crosslinking and oxidative side reactions. GelSH was generated through thiolactone ring opening using N-acetylhomocysteine thiolactone. The hydrogel mixture was prepared by combining GelSH (DS55) and GelNB (DS90) at a 1:1 molar ratio. To prevent spontaneous disulfide bond formation between thiol groups, tris(2-carboxyethyl)phosphine was added at 25 mol% relative to GelSH. For photopolymerization, 2 mol% - with respect to the NB content - lithium phenyl-2,4,6-trimethylbenzoylphosphine was incorporated as photoinitiator. Prior to UV exposure, the mixture underwent physical gelation by incubation at 4°C for 10 minutes. Subsequently, the gel was irradiated under a UV lamp (405nm, 3mW cm⁻² corresponding to 1800 mJ cm⁻²) for 10 minutes to induce thiol-ene crosslinking. To validate the biocompatibility, primary human intestinal fibroblasts were encapsulated at a density of 1 million cells/mL after which the gel was crosslinked and the cells were cultured within the hydrogel for a period of three weeks. Cell behaviour was monitored through brightfield microscopy, and cell viability and metabolic activity were quantified using the AlamarBlue assay.

Results: Both GelSH and GelNB displayed the expected chemical modification. NMR confirmed successful functionalization of gelatin derivatives, with characteristic peaks at 6.0, 6.2, 6.3 ppm corresponding to norbornene and thiol groups in GelNB, respectively. A ortho-phthalaldehyde assay quantified substitution degrees of 90% for GelNB and 55% for GelSH, indicating efficient modification and availability of reactive groups for crosslinking. Rheology tests on the 7.5% hydrogel blend showed intermediate viscosity (2,6 Pa·s) during thermal ramps and reached gel point rapidly under UV, with G' exceeding G'' within minutes. To assess the biocompatibility of the thiol-ene networks for cell encapsulation, fibroblasts were embedded within the GelNB-GelSH hydrogels. Encapsulated fibroblasts maintained their viability and preserved their spindle-shaped morphology as shown by brightfield and confocal imaging. Metabolic activity increased over time, suggesting proliferation within the bioink, indicating a good cellular compatibility.

Conclusions: These initial results illustrate that the developed thiol-ene crosslinked GelNB-GelSH hydrogel is biocompatible with intestinal fibroblast growth, and well-suited as a bioink platform for intestinal tissue engineering and future bioprinting applications.

ALTERATIONS IN CIRCULATING ADVANCED GLYCATION END PRODUCTS AFTER INITIATION OF BIOLOGICAL THERAPY IN INFLAMMATORY BOWEL DISEASE. E. Vissers (1), J. Wellens (1), C. Caenepeel (1), M. Ferrante (2), B. Verstockt (2), S. Vermeire (2), J. Sabino (2) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism, Translational Research in Gastrointestinal Disorders (TARGID), [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Advanced glycation end products (AGEs) are formed from a non-enzymatic reaction between reducing sugars and proteins, and can either be generated in the body or introduced through diet and smoking. AGEs are suggested to promote inflammation and oxidative stress, and influence treatment resistance in inflammatory bowel diseases (IBD)(Van der Lugt T et al. *Nutrients*. 2020.).

Aim: The aim of this study was to further explore the association of serum AGEs with IBD disease activity and response to biological therapy.

Methods: This retrospective study included patients with IBD initiating biological therapy (n=75), from a previously established cohort (Caenepeel C et al. *Gastroenterology*. 2024.). Therapy response was determined through endoscopic evaluation at week 14 for patients with ulcerative colitis (UC) (n=36), and at week 24 for patients with Crohn's disease (CD) (n=39). For UC, endoscopic improvement was defined as endoscopic Mayo score (EMS) ≤ 1 , with at least a 1-point decrease from baseline. For CD, endoscopic improvement was defined as simple endoscopic score for CD (SES-CD) ≤ 3 (SES-CD 0 for patients starting with SES-CD 3) and/or absence of ulceration. Serum samples were taken at baseline (w0) and after therapy outcome evaluation. Three AGEs were measured in serum using mass spectrometry: carboxymethyl-lysine (CML), N-(5-hydro-5-methyl-4-imidazolone-2-yl)-ornithine (MG-H1), and pyrraline (Pyr).

Results: The median age of our cohort was 32.1 years old (CD: 26.1 (IQR 23.1-33.8); UC: 39.7 (IQR 28.1-50.0)), with a median disease duration of 5.1 years (CD: 5.5 (IQR 1.8-12.4); UC: 4.9 (IQR 1.7-10.4)). Thirty patients started anti-TNF therapies (10 CD, 20 UC), 30 patients started vedolizumab (14 CD, 16 UC), and 15 CD patients started ustekinumab. About half of the patients responded to therapy (36 responders, 39 non-responders). At baseline, serum MG-H1 was significantly lower in patients with UC, compared to patients with CD ($p=0.0001$; Mann-Whitney test), with no differences in CML and Pyr. No significant difference in baseline levels of AGEs was observed between responders and non-responders. After therapy initiation, the levels of CML and MG-H1 decreased in CD, both in responders (CML: $p=0.0495$; MG-H1: $p=0.0432$) and non-responders (CML: $p=0.001$; MG-H1: $p=0.0253$) (2-way ANOVA). After receiving ustekinumab (UST), serum levels of CML significantly decreased in both responders ($p=0.0187$) and non-responders ($p=0.0015$) (2-way ANOVA). In CD and UC patients, serum levels of Pyr correlated positively with age (CD: $p=0.001$; UC: $p=0.001$) (spearman correlation analysis). In UC patients, serum MG-H1 negatively correlated with serum C-reactive protein ($p=0.003$) and the EMS ($p=0.013$) (spearman correlation analysis). In addition, serum Pyr negatively correlated with faecal calprotectin ($p=0.009$) and the EMS ($p=0.015$) (spearman correlation analysis). Lastly, there was a trend towards lower levels of MG-H1 ($p=0.0765$) and Pyr ($p=0.0556$) in patients with EMS 3, compared to EMS 0 (Kruskal-Wallis tests with post-hoc Dunn's tests).

Conclusions: Serum AGEs were not different between responders and non-responders to biological therapies, both at baseline and after treatment. We did observe differences between the serum AGEs in CD and UC patients, suggesting a different role for AGEs in both diseases. In UC patients, MG-H1 and Pyr correlated negatively with inflammatory markers, which should be further explored.

QUALITY OF LIFE AND DISEASE CONTROL OF IBD PATIENTS: INSIGHTS FROM THE BELGIAN COHORT OF THE MULTI-COUNTRY REAL-WORLD IBD-PODCAST STUDY. B. Verstockt (1), A. Colard (2), F. D'Heygere (3), J. Van Dongen (4), A. Despeghel (5), L. Ghys (5), C. Semanaz (5), D. Franchimont (6) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] Clinique MontLégia- CHC Groupe Santé, Liège, Belgium, Department of Gastroenterology, [3] AZ Groeninge, Kortrijk, Belgium, Department of Internal Medicine, [4] AZ Sint Maarten, Mechelen, Belgium, Department of Gastroenterology, [5] Abbvie, Wavre, Belgium, Medical, [6] Erasme Hospital, Brussels, Belgium, Department of Gastroenterology.

Introduction: Suboptimal disease control (SDC) in inflammatory bowel disease (IBD) might not only increase the risk of complications but also negatively impact quality of life (QoL). Consequently,

the updated “Selecting Therapeutic Targets in Inflammatory Bowel Disease” (STRIDE-II) recommendations also include restoration of QoL and reduction in disability as formal long-term targets. **Aim:** The IBD-PODCAST study estimated the proportion of IBD patients with SDC according to STRIDE-II in a real-world setting. This analysis estimates the prevalence of impaired QoL in Belgian IBD patients and examines associations with other clinical parameters, as well as with disease control assessment by both patient and physician.

Methods: IBD-PODCAST was a cross-sectional, non-interventional study including patients with ulcerative colitis (UC) and Crohn’s disease (CD) from 10 countries conducted between February 2022 and February 2023. SDC was assessed based on pre-defined indicators (red flags) from the STRIDE-II recommendations. These red flags included clinical parameters, biomarkers, endoscopy, other imaging and patient questionnaires such as the Short Inflammatory Bowel Disease Questionnaire (SIBDQ). The SIBDQ measured 10 items in four domains: bowel symptoms, emotional health, systemic symptoms and social function; impaired QoL was defined as SIBDQ<50. This analysis presents data from long-term treated Belgian patients (at least 13 to 24 weeks, depending on treatment type).

Results: The Belgian long-term cohort comprised 107 patients, 59 diagnosed with CD and 48 with UC. Red flags for SDC were observed in 55.9% (33/59) of patients with CD and in 41.7% (20/48) with UC. The most common red flag was impaired QoL (SIBDQ < 50), present in 40.7% (24/59) of patients with CD and in 16.7% (8/48) with UC. However, for patients with impaired QoL, ‘impaired QoL’ was the only red flag for 62.5% (15/24) of patients with CD and 37.5% (3/8) of patients with UC. When ‘impaired QoL’ appeared alongside other red flags, the most frequent additional red flags were extraintestinal manifestations (4/24), fistula presence (3/24), and steroid overuse (3/24) in CD and steroid overuse (4/8) and failure to achieve endoscopic remission (2/8) in UC. Of the 32 IBD patients with impaired QoL, only 14 were assessed as sub-optimally controlled by either their physician or themselves. Interestingly, only 6 were assessed as sub-optimally controlled by both simultaneously. Among the 22 patients who considered themselves adequately controlled despite having an SIBDQ<50, 5 had steroid overuse, 6 failed to achieve clinical remission, 2 failed to achieve endoscopic remission, and 2 had perianal disease. The more commonly used IBD-disk tool aligned with SIBDQ scores. Patients with SIBDQ<50 had a mean IBD-disk score of 50.7 (SD = 16.7), compared to 19.0 (SD = 14.1) for those with SIBDQ≥50. The IBD-disk scores also reflected disease control per STRIDE-II recommendations, with optimally controlled patients having an average score of 17.1 (SD = 12.7) and sub-optimally controlled patients having an average score of 41.1 (SD = 21.0).

Conclusions: These findings emphasize the significant challenge of achieving disease control and QoL in patients with IBD. Notably, patients with CD experienced higher quality of life impairment than those with UC. Additionally, nearly half of the patients with SIBDQ<50 also showed other SDC red flags, highlighting that routine QoL assessment is essential for effective disease management. Objective disease monitoring is key, since only a minority of patients with low SIBDQ scores were assessed as sub-optimally controlled by their physician or themselves. The IBD-disk tool shows strong concordance with SIBDQ scores and offers accessible QoL evaluation, making it a valuable alternative. While achieving disease control and preventing complications are central to IBD management, it is equally important to consider the impact of IBD on a patient’s overall wellbeing and daily life. Study limitations include lack of stratification according to patient therapeutic management. Red flags related to imaging may be underestimated as only 53% of patients underwent imaging during the 12-month window. QoL scores may be influenced by factors outside of the study scope, which can affect results even in healthy individuals. Quality of life measures are inherently subjective and cannot be expected to yield perfect scores, even among individuals without the disease.

-I45-

THE IMPACT OF COOKING METHODS ON INSULIN SENSITIVITY – FINDINGS FROM THE STEAMM STUDY. E. Vissers (1), J. Wellens (1), J. Vanderstappen (2), S. Hoekx (2), B. Verstockt (2), M. Ferrante (2), S. Vermeire (2), J. Sabino (2) / [1] KUL - University of Leuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism, Translational Research in Gastrointestinal Disorders (TARGID), [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction: Diet and metabolic dysfunction are both associated with IBD development and progression. Current dietary guidelines focus on ingredients, while cooking methods are overlooked. During thermal treatment of foods, advanced glycation end products (AGEs) can be formed, which are hypothesised to be involved in inflammation and metabolic diseases. Therefore, our research group conducted the STEAMM study, a randomized cross-over trial where healthy participants followed a high- and low-AGEs diet, which

contained identical ingredients but differed in cooking methods, and showed that cooking methods impact serum lipids and cholesterol, and faecal short-chain fatty acids (Wellens J et al. Cell Reports Medicine. 2025.).

Aim: Building on the STEAMM study, we aim to further explore the impact of a high- and low-AGEs diet on metabolic outcomes related to insulin sensitivity.

Methods: In a cross-over design, twenty healthy volunteers were randomly allocated to a high-to-low AGEs diet (HL) group or a low-to-high AGEs diet (LH) group, based on different cooking instructions. Fasting serum and faecal samples were taken at three timepoints: at baseline, after the first 2-week intervention period (T1), and after the second 2-week intervention period (T2). Serum levels of insulin, glucagon-like peptide 1 (GLP-1) and gastric inhibitory polypeptide (GIP) were determined by enzyme-linked immunosorbent assays (ELISAs). Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) was calculated from fasting insulin and glucose concentrations (Matthews DR et al. Diabetologia. 1985).

Results: Over the course of the study, weight (mean -1.8 kg, $p = 0.0005$), and fasting levels of serum insulin ($p=0.002$) and GLP-1 ($p=0.0004$) decreased across all participants (Friedman tests with post-hoc Dunn's tests), compared to baseline. In line, HOMA-IR was significantly lower after T2 compared to baseline ($p=0.006$) (Friedman test with post-hoc Dunn's tests). When separating the different groups, we observed a reduction of insulin ($p=0.032$), GLP-1 ($p=0.0009$) and HOMA-IR ($p=0.032$) in the HL group, while this was not significant in the LH group (Friedman tests with post-hoc Dunn's tests). Serum levels of GIP remained constant throughout the study. Spearman correlation analysis showed significant positive correlations between insulin levels and C-reactive protein ($p=0.027$), as well as carboxymethyl-lysine ($p=0.047$), a common dietary AGE. Faecal calprotectin was positively correlated with serum GIP ($p=0.001$) and pyrraline levels ($p=0.013$), another dietary AGE.

Conclusions: Fasting insulin levels and HOMA-IR decreased after the low-AGEs diet in the HL group, reflecting an overall improvement of metabolic function. Interestingly, serum levels of pyrraline were associated with faecal calprotectin. Overall, this data supports the inclusion of cooking methods in dietary guidelines for patients with IBD, but further research is needed to confirm this and provide mechanistic insights.

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-K01-

IMPROVEMENTS IN PRURITUS ARE ASSOCIATED WITH IMPROVEMENTS IN GROWTH IN PATIENTS WITH PROGRESSIVE FAMILIAL INTRAHEPATIC CHOLESTASIS: DATA FROM THE MARCH-ON TRIAL. E. Sokal (1), A. Miethke (2), A. Aqul (3), C. Lin (4), D. Mogul (5), T. Nunes (6), J. Turner-Rosenthal (7), M. Baek (8), P. Vig (7), R. Thompson (9) / [1] UCLouvain, Cliniques universitaires Saint-Luc, Belgium, Cliniques universitaires Saint-Luc, [2] Cincinnati Children's Hospital, United States, Medical Centre, [3] University of Texas Southwestern, Dallas, United States, Medical Centre, [4] Children's Hospital Los Angeles, Los Angeles, United States, Medical Centre, [5] Mirum Pharmaceuticals, Inc, United States, Scientific Affairs, [6] Mirum Pharmaceuticals, Inc, United States, Clinical Development, [7] Mirum Pharmaceuticals, Inc, United States, Medical Affairs, [8] Mirum Pharmaceuticals, Inc, United States, Biostats, [9] King's College Hospital London, London, United Kingdom, Institute of Liver Studies.

Introduction: Progressive familial intrahepatic cholestasis (PFIC) is a group of disorders resulting in disrupted bile composition and cholestasis leading to debilitating pruritus, growth deficits, vitamin deficiency, and progressive liver damage. Maralixibat, an IBAT inhibitor, is approved in the EU for the treatment of PFIC in individuals ≥ 3 months old. MARCH, a Phase 3 trial of maralixibat, achieved its primary and key secondary endpoints of pruritus and sBA reduction. Long-term maintenance of effect, including growth, for up to two years was observed in MARCH-ON, an open-label extension.

Aim: We report on the relationship between pruritus response and growth improvements in MARCH-ON.

Methods: Pruritus response was defined as a participant having ≥ 1 point reduction in ItchRO(Obs) from baseline to the average of the final 3-week periods of MARCH (Weeks 15-18, 19-22, 23-26). Height and weight Z-scores were analysed. Wilcoxon signed-rank test and rank sum test were used to determine CFB significance within groups and between groups.

Results: Sixty participants from the All-PFIC cohort in MARCH-ON were included in the analysis. Baseline characteristics were well-balanced between groups. Growth (mean [SD]) for the pruritus responders (height z-score: -1.8 [1.3]; weight-score: -1.2 [1.1]) and non-responders (height z-score: -2.6 [1.2]; weight z-score: -1.8 [1.5]) was stunted at Baseline. Thirty-seven participants met the pruritus responder criteria in the All-PFIC population and 23 were non-responders. Pruritus responders had a significant improvement in height (mean CFB [SE]: 0.4 [0.09]; $P < 0.0001$) and weight z-scores (CFB: 0.38 [0.07]; $P < 0.0001$) at Week 26, sustained out to 70 weeks of MRX treatment in MARCH-ON (height CFB: 0.53 [0.10]; $P < 0.0001$; weight CFB: 0.51 [0.15]; $P = 0.001$). Significant differences between pruritus responders and non-responders were sustained out to 70 weeks in height (CFB Δ : +0.63; $P = 0.0049$) and numeric improvements in weight (CFB Δ : +0.52; $P = 0.11$).

Conclusions: These consistent trends in growth for participants receiving maralixibat who were pruritus responders indicate a potential disease-modifying effect of maralixibat treatment in PFIC.

-K02-

MANAGEMENT OF PANCREAS DIVISUM IN CHILDREN: A REVIEW AND CASE SERIES. E. Wuyts (1), K. Van Hoeve (2), I. Hoffman (2) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Paediatrics, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Paediatric Gastroenterology.

Introduction: Pancreas divisum (PD) is a congenital malformation of the pancreatic ductal system and is frequently identified in children presenting with acute recurrent pancreatitis (ARP) or chronic pancreatitis (CP). Current evidence on Paediatric PD management is limited, heterogeneous, and lacks standardized recommendations.

Aim: To systematically map the available literature on the management of PD in children and to describe institutional experience from a retrospective case series at University Hospitals Leuven.

Methods: A narrative literature review was performed according to PRISMA-S guidelines, including studies published between January 2000 and July 2025 reporting management outcomes in patients < 18 years with PD. In parallel, a retrospective chart review was conducted of all children diagnosed with PD at University Hospitals Leuven between 2000 and 2024. Data on clinical presentation, diagnostics, interventions, complications, and follow-up were collected. In the case series, clinical success of the management strategy

was defined as $\geq 50\%$ reduction in annual pancreatitis episodes. Changes in median incidence before and after therapeutic ERCP were statistically evaluated.

Results: Fourteen studies involving 268 Paediatric PD patients were included. Eleven studies described ERCP outcomes ($n=230$), reporting clinical success rates ranging from 50% to 100% and complete symptom resolution from 0% to 100%. Three studies described surgical management ($n=19$), with clinical success ranging from 50% to 100% and complete resolution from 0% to 33.3%. When aggregating raw patient numbers descriptively—without formal pooling or statistical analysis—both ERCP and surgical cohorts showed symptomatic improvement in a substantial proportion of children, although heterogeneity in follow-up and outcome definitions limits comparability. The institutional cohort comprised nine patients; eight underwent ERCP and seven received therapeutic interventions, totaling 43 procedures. Technical success was 93%, and complications occurred in 25.5%, predominantly post-ERCP pancreatitis. Among the seven therapeutically treated patients, the median incidence of pancreatitis episodes decreased from 1.7 to 0.8 episodes per year (62% relative reduction), a statistically significant decrease (Wilcoxon signed-rank test, $p = 0.016$). Clinical success was achieved in 5 of 7 patients (71%), and complete symptom resolution in one patient (14%).

Conclusions: Evidence from the literature and institutional experience indicates that ERCP may reduce the burden of pancreatitis in selected children with PD, although complete symptom resolution is uncommon and procedure-related complications remain an important consideration. Surgical treatment is less frequently reported and generally reserved for refractory cases. The current body of evidence is limited by small retrospective studies and heterogeneous outcome definitions, underscoring the need for prospective Paediatric research using standardized measures.

-K03-

A KISS FROM BLUNT TRAUMA: PAEDIATRIC GASTRIC ULCERS AFTER BLUNT ABDOMINAL INJURY. L. Wijnants (1), I. Hoffman (2), K. Van Hoeve (2) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, General paediatrics, [2] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Department of Paediatric Gastroenterology and Hepatology and nutrition, University Hospitals Leuven, KU Leuven, Leuven, Belgium.

Introduction: Hollow viscus injuries, though rare in blunt abdominal trauma, carry significant morbidity and mortality (10–20%). Diagnosis is challenging, and delays can worsen outcomes. We report a 9-year-old girl presenting with hematemesis due to a trauma-induced gastric ulcer, one week after striking her epigastrium against a steering wheel in a golf cart collision.

Aim: To highlight the importance of maintaining a high index of suspicion for gastrointestinal injury in paediatric blunt trauma and underscores the critical role of timely diagnosis and intervention.

Case Report: The child presented to the emergency department with acute hematemesis (three times within two hours) and shock. Following the accident, she experienced only mild transient abdominal discomfort and required no analgesics. On arrival, she was pale, hypotensive (82/40 mmHg; $-1.7/-1.8$ SD) and tachycardic (120 bpm). Laboratory results showed haemoglobin of 7.5 g/dL (normal > 11.5 g/dL). Abdominal ultrasound was normal. Upper gastrointestinal endoscopy revealed two opposing antral ulcers, so-called “kissing ulcers”, one actively bleeding. Treatment with high-dose proton pump inhibitors, blood transfusion, and endoscopic hemoclip placement achieved definitive haemostasis without recurrence. Helicobacter pylori infection and hypergastrinemia were excluded. Follow-up endoscopy eight weeks later showed complete ulcer healing.

Discussion: Acute upper gastrointestinal bleeding remains a medical emergency, with peptic ulcer disease as a major cause. Children are more vulnerable to blunt abdominal trauma due to a thinner abdominal wall, a horizontally oriented diaphragm, and elastic ribs. However, gastric ulcers secondary to trauma are exceedingly rare—only four paediatric cases have been previously reported. Typically, they appear as “kissing ulcers” on opposite gastric walls, likely caused by compression of the stomach between the anterior abdominal wall and the spine during impact, which can lead to mucosal damage and, in severe cases, perforation. Ongoing erosion into deeper layers may cause delayed haemorrhage or perforation, as seen in this case. Diagnosis is often challenging due to nonspecific symptoms, often delayed presentation, and rarity. Early recognition, prompt endoscopy, and appropriate medical and endoscopic management are essential to prevent serious complications.

Conclusions: Trauma-induced gastric ulcers in children are rare but potentially life-threatening. This case highlights the importance of maintaining a high index of suspicion for gastrointestinal injury in paediatric blunt trauma and underscores the critical role of timely diagnosis and intervention.

-N01-

BELCHING AND RUMINATION ARE MORE PREVALENT IN PATIENTS WITH GASTROPARESIS-LIKE SYMPTOMS. H. Matheussen (1), F. Carbone (2), E. Colomier (2), J. Tack (2), AEGIS working group (3), T. Vanuytsel (2), K. Raymenants (2) / [1] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, TARGID, [2] KU Leuven, Leuven, Belgium, TARGID, [3] KU Leuven, Leuven, Belgium, AEGIS working group.

Introduction: Gastroparesis and gastroesophageal reflux disease (GERD) often coexist. In patients with refractory GERD, evaluation for gastroparesis is advised, as treatment with prokinetic agents may also help to alleviate reflux symptoms. Similarly, an overlap between gastroparesis and other upper gastrointestinal symptoms - such as belching and rumination - has been suggested yet remains under investigated.

Aim: This study aims to assess the relation between gastroparesis-like symptoms on the one hand and upper gastrointestinal symptoms such as rumination, belching and GERD on the other.

Methods: A retrospective analysis was conducted using data from the prospectively collected multicentre Asian European Gastrointestinal Symptom database (AEGIS). This cohort comprises 1,074 adult patients with a physician-confirmed diagnosis of at least one disorder of gut-brain interaction (DGBI) across six European and five Asian tertiary care centres. Based on UEG and international consensus (Schol et al., 2025), patients with gastroparesis-like symptoms were characterized by chronic nausea and vomiting at least once weekly, and early satiety and postprandial fullness at least twice weekly for six months. Heartburn was deemed significant when occurring at least twice per week. Rumination and belching were identified according to the Rome IV criteria. For patients for whom gastric emptying data were available (scintigraphy or gastric emptying breath test), gastroparesis was defined as having gastroparesis like symptoms with delayed emptying (cutoff as per local guideline). Comparisons between groups were performed using chi-square tests. Multivariate logistic regression was used to explore predictors with odds ratios to quantify their relevance. Unpaired t-test or Man-Whitney U test – in case of non-normally distributed data- was used to compare means.

Results: In this cohort, 66 patients had gastroparesis-like symptoms, rumination was present in 116, belching in 86, and heartburn in 219 patients. Median BMI was significantly lower in rumination patients with gastroparesis like symptoms compared to those without (20.6 kg/m² vs. 24.7 kg/m² (p=0.003)). The same was true for heartburn patients (20.6 kg/m² vs. 23.3 kg/m² (p=0.020)). The percentage women was significantly higher in those with gastroparesis-like symptoms for both rumination and belching patients (95.0% vs. 80.2% (p=0.040); 89.5% vs. 64.2% (p=0.035)). In a multivariate logistic regression, the odds of having rumination (OR 4.13 [2.35-7.27]), belching (OR 5.68 [3.16-10.22]) and heartburn (OR 2.94 [1.76-4.93]) were significantly higher in patients with gastroparesis-like symptoms compared to the total cohort. In a secondary multivariate logistic regression - with heartburn as the dependent variable -both rumination (OR 2.50 [1.66-3.78]) and belching (OR 2.01 [1.25-3.25]) were significantly associated. With rumination or belching as dependent variable their association was only borderline significant (OR 2.03 [1.14-3.63]).

Conclusions: As had previously been outlined for GERD, we demonstrate that gastroparesis-like symptoms in tertiary care patients are significantly associated with other upper gastro-intestinal symptoms such as belching and rumination. The pathophysiological basis and treatment implications of this overlap need to be addressed in future studies.

-N02-

DOSE REDUCTION OF BUDESONIDE IN EOSINOPHILIC OESOPHAGITIS : IS LESS ENOUGH? J. Verschaeete (1), J. Defrancq (1), C. Dilewyns (1), J. Tack (1), T. Vanuytsel (1), K. Raymenants (1), L. Wauters (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and Hepatology.

Introduction: Budesonide Orodispersible Tablets (BOT) are highly effective in the treatment of eosinophilic oesophagitis (EoE). While most studies focused on twice-daily (BID) dosing, we previously showed favourable outcomes with once-daily (OD) dosing in EoE (1). We also showed that BOT OD is more feasible than the viscous solution (2). BOT is reimbursed in Belgium since May 2024, with the possibility of OD maintenance therapy.

Aim: The aim of the present study was to evaluate the efficacy and safety of BOT 1mg OD following dose reduction from 1mg BID in patients with EoE.

Methods: We performed an observational study of BOT maintenance therapy in confirmed EoE patients at a tertiary care centre (UZ Leuven). Patients in remission after at least 3 months of BOT 1mg BID were followed after dose reduction to BOT 1mg OD for at least 6 months. We compared histological (peak eosinophil count (PEC) of <15 eosinophils per high-power field (eos/HPF)) and deep histological remission (PEC of <5 eos/HPF) before and after dose reduction. Changes in EoE Endoscopic Reference Scores (EREFS, remission defined as ≤ 2), Dysphagia Symptom Questionnaires (DSQ), EoE symptom Activity Index (EEsAI) and the Adult EoE Quality of Life Questionnaires (EoE-QoL-A) were also compared. Since Candida is the most common side effect of BOT, the clinical presence of oropharyngeal or oesophageal candidiasis was routinely assessed. The Index of Severity for EoE (I-SEE) score was determined at diagnosis and before and after dose reduction. This score includes symptoms, complications, inflammatory and fibrostenotic features to monitor disease severity (3). Data are presented as proportions or medians with interquartile ranges, with paired tests for proportions (McNemar) or continuous variables (Wilcoxon).

Results: A total of 36 EoE patients were included (23 male, age 30 (22-43.5) years and BMI 24.65 (21.52–27.60) kg/m²) after treatment with BOT 1mg BID for 109 (94-152) days. Of these patients, 22 were also assessed after dose-reduction to BOT 1mg OD for 179 (175-224) days. While a significant increase in PEC (0 (0-11) eos/HPF on 1mg OD vs. 0 (0-0) eos/HPF on 1mg BID, $P = 0.03$) was found after dose reduction, histological (80.95% on 1mg OD vs. 100% on 1mg BID, $P = 0.13$) and deep histological remission rates (66.67% on 1mg OD vs. 91.67% on 1mg BID, $P = 0.13$) were similar. Total EREFS scores remained low after dose reduction (0 (0-1) on 1mg OD vs. 0 (0-1) on 1mg BID, $P = 0.37$), with similar rates of endoscopic remission (90.48% on 1mg OD vs. 91.67% on 1mg BID, $P = 1$). The median scores for DSQ (0 (0-0) on 1mg OD vs. 0 (0-0) on 1mg BID, $n = 5$), EEsAI (27 (23-39) on 1mg OD vs. 17 (3-27) on 1mg BID, $n = 6$) and EoE-QoL-A (65.5 (55-78.75) on 1mg OD vs. 76 (51-88) on 1mg BID, $n = 7$) were similar after dose reduction. I-SEE scores were 7 (5-8.5) at diagnosis and significantly increased after dose reduction (1 (0-1.5) on 1mg OD vs. 0 (0-1) on 1mg BID, $P < 0.05$). In contrast, a trend for a lower incidence of Candida was found after dose reduction (19.05% on 1mg OD vs. 38.89% on 1mg BID, $P = 0.07$).

Conclusions: Dose reduction of BOT 1mg BID to 1mg OD is clinically feasible as maintenance therapy for EoE, with only few patients losing histological remission and overall lower rates of Candida. However, the subtle increase in peak eosinophils and severity scores suggest that a longer follow-up is needed to detect potential loss of response beyond 6 months.

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-N03-

FUNCTIONAL DYSPEPSIA/EPIGASTRIC PAIN SYNDROME: ARE EPIGASTRIC PAIN AND EPIGASTRIC BURNING CONNECTED OR SEPARATE SYMPTOMS? AN ANALYSIS FROM THE AEGIS STUDY. I. El Aissaoui (1), J. Lehoucq (1), F. Carbone (2), K. Van den Houte (1), A. AEGIS working group (2), J. Tack (2)/[1] Translational Research Centre for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, *Gastroenterology*, [2] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, *Gastroenterology*.

Introduction: Functional dyspepsia with epigastric pain syndrome (FD-EPS) is defined by the Rome IV criteria as the presence of epigastric pain and/or burning, without distinguishing between these two symptom types. It is unknown whether pain and burning occur simultaneously or separately in EPS patients. The latter case could indicate heterogenous underlying pathophysiology and potentially meaningful differences in symptom severity and treatment response.

Aim: To evaluate differences in symptom severity among FD-EPS patients experiencing epigastric pain only, epigastric burning only or both, and to investigate whether this variation is influenced by coexisting conditions and factors such as irritable bowel syndrome (IBS), postprandial distress syndrome (FD-PDS), heartburn, meal intake, antacid and proton pump inhibitor (PPI) use.

Methods: A total of 300 consecutive FD-EPS patients were recruited from eleven specialist care centres across Europe ($n = 193$, 64.3%) and Asia ($n = 107$, 35.7%). All participants completed a comprehensive set of questionnaires, including the Rome IV diagnostic questionnaire, pain and/or burning symptom severity and

frequency, and questions regarding relationship of symptoms to meal intake and potential relieving factors. Patients were categorised into three groups based on their reported symptoms: pain only (P), burning only (B), or both (P+B). Differences in symptom severity were analysed across subgroups, along with comparisons of IBS, FD-PDS and heartburn overlap, meal intake, antacids and PPI use. All p-values were adjusted with Bonferroni-correction.

Results: Of the 300 EPS patients, 150 (50.0%) reported P, 29 (9.7%) B, and 121 (40.3%) experienced P+B. In this sample, approximately 75% were female, with ages ranging from 18 to 74 years (median: 40) and BMI values from 12.98 to 40.00 (median: 22.89). There were no significant differences between the groups for gender, age, BMI and symptom frequency scores. P+B patients had significantly higher PHQ-9 ($p=0.033$), GAD-7 ($p<0.01$) and PHQ-12 scores ($p=0.021$) than B. Additionally, PHQ-12 scores were also significantly higher in the P+B group compared to P ($p<0.01$). Symptom severity was also significantly higher in P+B than P ($p<0.001$) or B ($p<0.001$). No significant differences were observed in the prevalence of IBS overlap among the groups. However, overlap with PDS was significantly higher in P+B compared to P (66% vs. 48%, $p=0.013$). Similarly, heartburn overlap and heartburn+IBS overlap were more common in P+B than P (20.7% vs. 4.7%, $p<0.001$ and 2.7% vs. 13.2%, $p<0.01$ respectively). Symptom severity did not differ significantly among patients with overlapping disorders. No significant differences were found in the proportion of meal-related versus meal-unrelated symptoms across groups, nor in severity between these subgroups. Furthermore, there was no significant difference in severity between patients taking PPIs (20.6%) and those not taking PPIs. However, compared to P, B ($p<0.01$) and P+B ($p<0.0001$) reported significantly greater symptom relief with antacids.

Conclusions: EPS is a heterogeneous condition with the largest subgroups reporting pain only or both pain and burning, and isolated epigastric burning is uncommon. This abstract aimed to explore differences among these symptom-based subgroups. The response to antacids and overlap with heartburn suggest that B may represent an acid-related symptom, but this requires confirmation in prospective mechanistic and treatment trials. Overlapping disorders did not correspond to a higher symptom severity. However, patients with both pain and burning have greater symptom severity and psychological comorbidity. Future research will need to study whether the underlying pathophysiology and the treatment responses differ in these subgroups.

-N04-

EVALUATION OF DELAYED GASTRIC EMPTYING (GASTROPARESIS) AS A MARKER OF DISEASE SEVERITY IN SYSTEMIC SCLEROSIS. F. Felix Tellez (1), A. Guillen del Castillo (2), P. Claudia (3), A. Ariadna (1), C. Barber (1), C. Malagelada (1), L. Polo-Figueras (1), L. Triginer (2), C. Codina (2), M. Hughes (4), J. Serra (1), C. Simeon Aznar (2), Z. McMahan (5), L. Alcalá González (1) / [1] Fundació Hospital Universitari Vall d'Hebron - Institut de Recerca, Barcelona, Spain, Digestive System Research Unit, Department of digestive diseases, [2] Fundació Hospital Universitari Vall d'Hebron - Institut de Recerca, Barcelona, Spain, Autoimmune Diseases, Internal Medicine, [3] UTHealth Houston, Houston, United States, Department of Paediatrics, [4] Manchester Academic Health Science Centre, Manchester, United Kingdom, Division of Musculoskeletal and Dermatological Sciences, [5] UTHealth Houston, Houston, United States, Department of Medicine, Division of Rheumatology.

Introduction: Gastrointestinal involvement is one of the most prevalent and clinically relevant complications of systemic sclerosis, affecting up to 90% of patients and contributing substantially to morbidity. Although esophageal dysmotility has been well characterized, gastric dysmotility—particularly gastroparesis—remains insufficiently studied, and its clinical implications are poorly defined. At our centre, all patients with systemic sclerosis undergo a comprehensive evaluation of gastrointestinal involvement at the time of inclusion, including high-resolution esophageal manometry, regardless of symptoms.

Aim: We aimed to determine whether gastric dysmotility is associated with distinct clinical phenotypes, immunological features, esophageal motor patterns, and adverse outcomes in SSc.

Methods: We conducted a single-centre retrospective cohort study in a prospectively maintained systemic sclerosis database. Consecutive adult patients diagnosed with systemic sclerosis and fulfilling ACR/EULAR 2013 and/or LeRoy criteria were included. Patients who underwent both high-resolution esophageal manometry (HREM) and gastric emptying scintigraphy (GES) at baseline between January 2015 and March 2024 were included. GES was performed using a standardized solid meal protocol, and gastric dysmotility was defined as moderate-to-severe delayed gastric emptying ($\geq 20\%$ retention at 4 hours). Demographic,

clinical, immunologic, and capillaroscopic data were obtained from the prospective registry. Esophageal motility was classified according to Chicago Classification 4.0 and gastrointestinal symptom burden at inclusion was evaluated using the UCLA SCTC GIT 2.0 questionnaire (a validated, patient-reported outcome measure specifically designed for systemic sclerosis. It assesses gastrointestinal symptoms across 7 sub-domains; reflux, distension/bloating, diarrhea, faecal soilage, social functioning, GI well-being, constipation, and overall GI burden). Outcomes included systemic sclerosis-related mortality and/or lung transplantation. Kaplan–Meier survival curves, and Cox proportional hazards models were applied.

Results: Ninety-four patients were included (mean age 48 ± 12 years; 81% women). Gastric dysmotility was identified in 33 patients (35%), with 21 showing moderate delay (20–35% retention at 4h) and 12 severe delay ($>35\%$ retention at 4h). The remaining 61 patients (65%) had normal ($<10\%$ retention at 4h, $n=46$) or mildly delayed (10–19% retention at 4h, $n=15$) gastric emptying. Patients with gastric dysmotility had a significantly higher prevalence of interstitial lung disease (63.6% vs. 30.3%, $p=0.024$) and were more likely to exhibit late pattern on nailfold capillaroscopy (36.4% vs. 18.0%, $p=0.030$). Gastric dysmotility clustered with more severe esophageal dysmotility. Patients with gastric dysmotility had a significantly higher prevalence of absent esophageal contractility (75.8% vs. 45.9%, $p=0.005$). Conversely, ineffective esophageal motility was only found in patients without gastric dysmotility (29.5% vs. 0%, $p<0.001$). Evaluating the auto-antibodies profile, gastric dysmotility was significantly less frequent in patients with anti-centromere antibodies (27.3% vs. 55.0%, $p=0.009$) and more common in those with anti-U1-RNP antibodies (15.6% vs. 1.7%, $p=0.011$). In multivariable models, Anti-centromere positivity remained independently protective against gastric dysmotility (fully adjusted aOR 0.2, 95% CI 0.1–0.8; $p=0.018$), while the association with anti-U1RNP persisted in sensitivity analyses among patients without myopathy. We found no differences regarding gastrointestinal symptom severity (total SCTC GIT 2.0 score, 1.10 [0.88–1.59] vs 0.91 [0.76–1.29], $p=0.272$) or in any sub-domain (all $p>0.05$) between patients with and without gastric dysmotility. Over a mean 2.8 ± 1.7 years of follow-up (260 person-years), 16 patients (17.0%) reached the composite endpoint (7 deaths, 12 lung transplants; with 3 post-transplant deaths). Event-free survival was significantly worse in patients with gastroparesis (log-rank $p<0.001$). In unadjusted Cox regression, gastric dysmotility was strongly associated with adverse outcomes (HR =6.47, 95%CI: 2.09–20.10, $p=0.001$), which remained significant after adjustment for the presence of interstitial lung disease and esophageal absent contractility (HR=4.23, 95%CI: 1.25–14.33, $p=0.020$).

Conclusions: Among patients with systemic sclerosis, gastric dysmotility (moderate - to severe delayed gastric emptying) is associated with a distinct immunological profile and is independently linked to an increased risk of adverse outcomes. These findings highlight the importance of objective gastric function testing for risk stratification in patients with systemic sclerosis, regardless of gastrointestinal symptoms.

-N05-

HIDDEN HELICOBACTERS: UNMASKING NON-HELICOBACTER PYLORI HELICOBACTER (NHPH) INFECTION IN UNINVESTIGATED DYSPEPSIA. J. Verstraelen (1), C. Van Steenkiste (2), B. Oosterlinck (1), A. Smet (1), H. De Schepper (3), B. De Winter (1) / [1] University of Antwerp, Antwerp, Belgium, Laboratory of Experimental Medicine and Paediatrics, [2] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, AZ Maria Middelaers - Gastroenterology and Hepatology, [3] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology and Hepatology.

Introduction: According to the Rome IV criteria, functional dyspepsia can be subdivided into epigastric pain syndrome (EPS) and postprandial distress syndrome (PDS). Symptoms range from early satiation and bloating to epigastric burning and vomiting. Patients presenting with dyspeptic symptoms are initially classified as having “uninvestigated dyspepsia” until structural or infectious causes of their symptoms are excluded. A common and treatable cause of dyspepsia is an infection with *Helicobacter* (H.) *pylori*. Other spiral-shaped gastric non-*Helicobacter pylori* *Helicobacter* species (NHPH) naturally colonizing the stomach of domesticated animals, have also been demonstrated to colonize the human gastric mucosa. These zoonotic agents have been described in patients with chronic gastritis, peptic ulcer disease and mucosa-associated lymphoid tissue lymphoma. Unlike H. *pylori*, NHPHs are not detected by standard non-invasive testing or routine histology due to their focal and patchy colonization pattern, underestimating their true prevalence in the human population. The current most accurate test for the diagnosis of gastric NHPHs is molecular testing combined with sequencing. Therefore, investigating the prevalence of NHPH in patients with uninvestigated dyspepsia may provide new insights into this functional gastric disorder, as these bacteria could represent a hidden and potentially treatable infectious cause.

Aim: To investigate the prevalence of NHPH infections in patients with uninvestigated dyspepsia.

Methods: This prospective, multicentric study included patients with dyspeptic symptoms and who tested negative for *H. pylori* in a previous gastroscopy. Gastric biopsies were collected from the inflamed (if present) and non-inflamed gastric antrum or corpus for DNA extraction purposes. Helicobacter genus- and species-specific qPCR assays were performed using 16S rRNA gene- and urease gene-based primers. The presence of the following gastric Helicobacter species was tested: *H. ailurogastricus*, *H. bizzozeronii*, *H. heilmannii*, *H. felis*, *H. salomonis*, *H. suis* and *H. pylori*.

Results: A total of 42 participants were included in this study. The median age was 49 years (IQR 28 years), and the median BMI was 25,9 (IQR 6,2). Thirty-four participants (81%) were female. Based on their symptoms, 21 patients (50%) were classified with EPS, 3 (7%) with PDS, and 18 patients (43%) met the Rome IV criteria for both subtypes. Biopsies were taken from both healthy and inflamed tissue, predominantly from the antrum, only two biopsies were collected from the corpus. The gastric mucosa showed discrete to low-grade inflammation in 26 participants, while the mucosa appeared healthy in the other 16 patients. A total of 15 participants (35,7%) tested positive for one or multiple NHPHs. Specifically, ten patients were infected with *H. suis*, seven with *H. felis*, six with *H. salomonis* and two with *H. ailurogastricus*. The gastric mucosa appeared macroscopically normal in six of these NHPH positive patients. Despite exclusion of patients with a previous *H. pylori*-infection, nine patients had an infection with *H. pylori* (21,4%) and 8 of these patients had a co-infection with at least one NHPH. The routine testing missed *H. pylori* in 4 of the 9 cases (44,4%).

Conclusions: NHPH infections were detected in patients with uninvestigated dyspepsia, both in mono-infection as in co-infection with *H. pylori*. qPCR detected more *H. pylori* infections than the routine histology, which indicates that some patients currently classified as having functional dyspepsia may actually be infected with a treatable infection. These findings highlight the need for further research to determine whether eradication of NHPH can improve patient symptoms, as these infections may represent an overlooked cause of dyspepsia. Additionally, the sensitivity of qPCR testing proved to be superior to the routine histology, which suggests an optimization in diagnostic practice for a more accurate detection, including broader screening for gastric Helicobacter species.

-N06-

THE EFFECT OF STOPPING LONG-TERM INAPPROPRIATE PPI THERAPY ON HEALTHCARE RESOURCE UTILIZATION: FINDINGS FROM THE PEPPER TRIAL. J. Scheepers (1), J. Tack (2), F. Carbone (2), K. Van den Houte (3) / [1] KUL - University of Leuven, Leuven, Belgium, TARGID, [2] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Translational Research Centre for Gastrointestinal Disorders, [3] KU Leuven, Leuven, Belgium, Translational Research Centre for Gastrointestinal Disorders.

Introduction: Inappropriate long-term use of proton pump inhibitors (PPIs) is a growing concern, with estimates of up to 70% of cases lacking a valid indication. This overuse may increase healthcare costs and expose patients to unnecessary risks and drug interactions.

Aim: To evaluate the impact of stopping long-term inappropriate PPI therapy on the utilization of drugs and healthcare resources.

Methods: Belgian general practitioners (GPs) recruited long-term PPI users without a strict medical indication. Demographics, PPI use (dose and duration) and medical history were collected at baseline. We used a Health Resource Utilization questionnaire to collect upper gastrointestinal-related healthcare utilization and prescription/over-the-counter (OTC) drug purchases over a 6-month recall period before PPI deprescription and after a one-year follow-up period. At follow-up, patients were classified as successfully deprescribed if PPI intake was <4 days/month. Patients were classified as unsuccessfully deprescribed if the PPI intake was ≥4 days/month, thereby including both chronic and on-demand PPI intake. Statistical significance ($p < 0.05$) was assessed using the Kruskal-Wallis and Chi-square tests. All costs and visits are reported per 6-month period. Results are presented as mean ± SD.

Results: A total of 665 patients (60±14 years; BMI 28±5 kg/m²; 60% female) were included by 61 GPs. Of these, 437 patients have now completed the trial, with 285 patients classified as successfully deprescribed, while 152 were unsuccessful. Baseline healthcare utilization included 219 GP visits and 50 gastroenterologist visits in the prior 6 months. At the end of follow-up, there was a significant decrease in GP visit frequency between baseline and the unsuccessful group (37/152, $p = 0.04$), but an increase in gastroenterologist visits (25/152, $p = 0.0006$). In addition, significantly fewer visits to both GPs and gastroenterologists occurred

in successful patients (GP: 27/285; gastroenterology: 11/285) compared to baseline and the unsuccessful group (both $p < 0.0001$). A significant increase in investigations (gastroscopy, CT abdomen, lab tests,...) is noted in the unsuccessful group, compared to baseline and the successful patients (both $p < 0.0001$). Medication costs at baseline averaged €40 per capita for prescriptions and €3 for OTC drugs. At follow-up, costs for unsuccessful patients decreased for prescriptions (€32 per capita, $p = 0.0031$), but remained similar for OTC drugs (€6 per capita). Successfully deprescribed patients showed a significant reduction in prescription costs (€1 per capita; $p < 0.0001$ vs baseline and unsuccessful group) but also a significant increase in OTC costs compared to baseline and the unsuccessful group (€11 per capita; $p < 0.0001$ and 0.04, respectively). No significant differences were observed in other healthcare expenses (e.g., dietitians, acupuncture, cognitive behavioural therapy,...).

Conclusions: Deprescribing inappropriate long-term PPI therapy significantly reduces prescription drug purchases and healthcare visits, which are both largely reimbursed by the Belgian healthcare system. This represents a meaningful decrease in (unnecessary) federal healthcare expenditure. However, this reduction is partially compensated by an increase in OTC medication costs, which must be paid out-of-pocket by patients. These findings underscore the importance of considering both public and patient-level financial implications when implementing deprescribing strategies.

-N07-

A CROSS-CULTURAL STUDY ON THE PERCEPTION OF PERCEIVED STOOL BLOCKAGE IN PATIENTS WITH DISORDERS OF GUT-BRAIN INTERACTION. A SUB-ANALYSIS OF THE AEGIS DATABASE. C. Van de Bruaene (1), F. Carbone (1), E. Colomier (1), M. Van Den Houte (2), K. Raymenants (1), C. von Muhlenbrock (3), B. Broeders (1), K. Van den Houte (1), T. Vanuytsel (1), J. Tack (1) / [1] Translational Research Centre for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism (Chrometa), [2] Translational Research Centre for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Department of Chronic Diseases and Metabolism (Chrometa), the Laboratory for Brain-Gut Axis Studies (LaBGAS), [3] Universidad de los Andes, Santiago, Chile, Departamento de Medicina Interna.

Introduction: A feeling of stool blockage during defecation is a Rome IV criterion for functional constipation (FC). However, many individuals who do not meet these criteria intermittently experience difficulty passing stool, which may promote maladaptive toileting behaviors such as excessive straining. The mechanisms underlying this perception remain poorly understood.

Aim: To identify factors associated with the feeling of stool blockage in patients reporting difficulty passing stool in $>25\%$ of bowel movements, and to compare findings between Eastern and Western populations. Associations with non-gastrointestinal (GI) somatic symptoms, anxiety, depressive symptoms, and GI symptom burden were evaluated using PHQ-12, GAD-7, PHQ-9, PAGI-SYM, and IBS-SSS scores.

Methods: In the AEGIS database, 1074 adults with disorders of gut-brain interaction (DGBIs), diagnosed by their physician, were recruited from 11 tertiary neurogastroenterology centres (6 Europe, 5 Asia) between May 2021–April 2023. Participants completed the Rome IV questionnaire (including extra stool-passage difficulty items) and symptom scales. Group comparisons used non-parametric median tests for continuous and chi-square or Fisher's exact tests for categorical variables. Multivariable logistic regression was applied to adjust for potential confounders. A $p < 0.05$ was considered statistically significant.

Results: Of 1074 patients, 372 (34.6%) reported difficulty passing stool; only 109 (29.3%) also met criteria for FC. The most frequently reported reasons for difficulty passing stool were: perceived feeling of stool getting stuck during defecation (61.3%), too hard (59.4%), too big (32%), too dry (27.2%), too painful to pass (25.5%), absence of urge feeling (17.7%), perceived weak propulsion force (15.9%), too thin (7.8%), or other (3.8%) in descending order. Regardless of meeting FC criteria, patients with blockage were younger (median 38 vs 43 years, $p = 0.003$) and more often female (77.5% vs 60.5%, $p < 0.001$). Prevalence was lower in Eastern than Western centres (26.4% vs 51.6%, $p < 0.001$). Eastern patients more often cited dry stool or weak propulsion (41.6% vs 19.8% and 31.2% vs 8.1%, both $p < 0.001$), whereas Western patients more often described a sensation of stool getting stuck and pain during defecation (67.2% vs 49.6% and 31.2% vs 14.4%, both $p < 0.001$). PPI/PCAB and antidepressant use were associated with dry stools (37.8% vs 24.3%, $p = 0.02$; 52.2% vs 25.4%, $p = 0.005$). Patients reporting blockage had higher PHQ-12, PHQ-9, GAD-7, PAGI-SYM, and IBSSS scores (all $p < 0.001$), indicating greater somatic, depressive, anxious, and GI symptom burden. After multivariable adjustment, only the PAGI-SYM remained significantly higher overall and within both regional subgroups ($p < 0.001$).

Conclusions: A feeling of stool blockage is common in DGBI and extends beyond FC. Interestingly, it most often reflects a sensation of stool getting stuck despite adequate effort, rather than being related to stool hardness or size. This symptom is not only linked to stool characteristics, but also medication use, psychological factors, and GI symptom burden, with notable East–West differences. These findings highlight the multifactorial nature of defecatory symptoms and support a holistic, biopsychosocial approach to management.

-N08-

METHANE PRODUCTION DURING HYDROGEN BREATH TEST: EVALUATION OF SYMPTOM PROFILE AND ADDED VALUE TO DIAGNOSE LACTOSE INTOLERANCE. C. Gulkilik (1), L. Brown (2), M. Houinsou Hans (3), H. Louis (1) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Hepatopancreatology and Digestive Oncology, [2] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Faculty of Medicine, [3] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Biomedical Research.

Introduction: The hydrogen breath test (H₂BT) is routinely used to diagnose lactose intolerance by measuring exhaled hydrogen (H₂) and methane (CH₄) concentrations after lactose oral administration in patients with digestive symptoms. In some individuals, an increased abundance of methanogenic archaea leads to CH₄ production. Previous studies have suggested an association between a methanogenic profile and constipation, as methane may slow intestinal motility. However, data remain limited regarding whether methanogenesis is linked to other gastrointestinal symptoms, and whether methane dosage helps to diagnose lactose intolerance.

Aim: To determine whether CH₄ production is associated with a distinct symptom profile, and to evaluate the diagnostic performance of measuring CH₄ levels for lactose intolerance during an H₂BT.

Methods: A retrospective study was conducted on 427 adult patients who underwent an H₂BT in a tertiary hospital between January 2023 and November 2024. Collected data included demographic characteristics, usual symptoms before performing H₂BT (scored 0 to 5), symptoms reported during the test (scored 0 to 5) and breath gas levels (H₂ and CH₄). The presence of a symptom was defined with a score ≥ 1 , and a symptom with moderate or severe intensity with a score ≥ 3 . A methanogenic profile was defined when a CH₄ value was ≥ 10 ppm. Patients were divided into two groups: methanogenic and non-methanogenic. Statistical analyses were performed using chi-squared and Mann–Whitney tests, with a significance threshold of $p < 0.05$.

Results: Among the 427 patients, 123 (28.8%) exhibited a methanogenic profile. The median age was 35 years, and 69.6% were female. No significant difference was observed between groups regarding age, sex, or BMI. Baseline and peak CH₄ levels were significantly higher in the methanogenic group ($p < 0.0001$). Hydrogen levels were slightly lower in the methanogenic group, but without statistical significance. Analysis of the usual symptoms reported before the H₂BT revealed that constipation was significantly more frequently reported among methanogenic patients (62.6% vs. 52%, $p = 0.046$). No other symptom, such as bloating, abdominal pain, flatulence, diarrhoea, nausea, vomiting, belching, or borborygmi, was significantly associated with the methanogenic profile. Moderate or severe constipation was more common in the methanogenic group (38.2% vs. 28.3%, $p = 0.045$). The median scores of bloating and flatulence were higher in the methanogenic group than in the non-methanogenic group, however not significantly. The distribution of H₂BT conclusions (lactose intolerance, lactose malabsorption, lactose sensitivity without malabsorption, or negative test) did not differ between methanogenic and non-methanogenic patients ($p = 0.88$). Lactose intolerance was diagnosed based on H₂ measurement in 127 of the 427 patients (29.7%). Among the 109 patients classified as having lactose sensitivity without malabsorption (symptoms occurring during H₂BT without an H₂ rise), 29 (26.6%) were methanogenic. Of these, only 5 (1.2% of the total cohort) exhibited a CH₄ increase ≥ 10 ppm during the test, suggesting possible lactose intolerance masked by H₂ consumption from methanogenic activity. Methane levels of the other 24 patients were high before lactose administration, and did not rise during the test. Including CH₄ measurement therefore allowed the identification of approximately 1% additional lactose intolerance cases.

Conclusions: Nearly one-third of patients undergoing H₂BT had a methanogenic profile. Constipation was the only symptom significantly associated with methane production, which supports previous evidence that methane may inhibit intestinal motility. The added diagnostic value of methane measurement to diagnose lactose intolerance during H₂BT appears to be limited in comparison with H₂ measurement.

EFFICACY OF LACTOSE REDUCTION IN IRRITABLE BOWEL SYNDROME AND RECURRENT ABDOMINAL PAIN: A SYSTEMATIC REVIEW OF THE LITERATURE. L. Van den Eeckhaut (1), M. Van der Merwe (1), C. Melchior (2), G. Gourcerol (3), Y. Vandeplas (4), K. Huysentruyt (4), S. Kindt (1) / [1] University Hospital Brussels, Vrije Universiteit Brussel, Belgium, Gastroenterology and hepatology, [2] Université de Rouen, INSERM, Normandie Univ, CHU Rouen, Rouen, France, Gastroenterology, [3] Université de Rouen, INSERM, Normandie Univ, CHU Rouen, Rouen, France, Physiology, [4] KidZ Health Castle, UZ Brussel, Vrije Universiteit Brussel (VUB), Brussels, Belgium, Jette, Belgium, Kindergastroenterologie, hepatologie en nutritive.

Introduction: Lactose intolerance (LI), irritable bowel syndrome in adults (IBS) and recurrent abdominal pain (RAP) in children are frequently diagnosed worldwide. When confronted with abdominal pain in the absence of alarm symptoms, LI is frequently suspected by patients or their parents, and healthcare professionals. However, it is unclear whether a positive lactose test (LBT) predicts the outcome of a lactose free diet in these patients. Moreover, guidelines recommend against systematic testing.

Aim: Therefore, this systematic review aimed to assess the effects of dietary reduction in lactose on symptoms, quality of life and healthcare visits in IBS and children with recurrent abdominal pain.

Methods: PubMed, Cochrane library, Embase and Lilacs were searched for studies on IBS and RAP investigating the effect of a reduction of dietary intake of lactose for at least 4 weeks on abdominal pain, stool characteristics, bloating and distension, and quality of life. No restriction in language, publication type or data limit were applied. Four reviewers independently screened the abstracts for eligibility. Risk of bias was assessed with RoB2.0 by 2 reviewers. Disagreement were resolved by consensus or consulting with a senior investigator.

Results: Literature search revealed 973 studies, of which 18 met eligibility criteria based on the title and abstract. Upon review of full-text articles, 3 studies in adults (450 patients) and 6 studies in children (420 patients) were retained for data extraction. LBT was performed in all studies. All but one study prospectively compared patient cohorts. One study assessed RAP in children retrospectively. IBS was defined by Manning criteria in 2, and Rome II criteria in 1 study. RAP was defined clinically. Except for one study in adults comparing the effect of a lactose free diet irrespectively of the result of the LBT, only patients with a positive LBT were subjected to dietary intervention in 2/3 studies in adults and 6/6 studies in children. No control group was included in 2/3 and 3/6 of the studies in adults and children respectively. None of the studies compared symptomatic evolution based on validated questionnaires. Improvement in pain was reported in more than half the subjects in 2 of the studies in adults, and in all the studies on RAP. The risk of bias was high for all studies. No study assessed quality of life.

Conclusions: Current evidence in support of dietary lactose reduction in patients with IBS and RAP is limited due to the use of old criteria, the absence of a valid comparator group and poorly defined outcomes. A positive LBT was associated with improvement of pain after dietary lactose reduction. Overall, studies suffered from a high risk of bias. Future studies on the role of lactose restriction in IBS and RAP should recruit patients based on current diagnostic criteria, and assess outcome by validated measures, preferentially applying a randomised controlled design.

GLOBAL IBS, LOCAL PATTERNS: REGIONAL VARIABILITY IN PAIN, BLOATING, AND DAILY-LIFE IMPACT IN ASIAN AND WESTERN EUROPEAN PATIENTS FROM THE AEGIS EPIDEMIOLOGY SURVEY. C. von Muhlenbrock (1), F. Carbone (2), E. Colomier (2), C. Van de Bruaene (2), T. Vanuytsel (2), J. Tack (2) / [1] Translational Research Centre for Gastrointestinal Disorders (TARGID), Lab for Enteric Neuroscience (LENS), KU Leuven, Leuven, Belgium, Gastroenterolgy, [2] Translational Research Centre for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Gastroenterology.

Introduction: Regional differences in IBS may shape symptom perception, diagnosis, and treatment. Bloating, stress, and anxiety strongly relate to IBS severity. Using validated symptom questionnaires and pictograms can help identify sociocultural and physiological modifiers of symptom burden and improve region-specific management.

Aim: To compare IBS subtypes in Asian versus Western patients and assess its association with overall IBS severity, as well as evaluate differences in symptom severity scores between both groups.

Methods: Adults over 18 years old who met Rome IV criteria for IBS were interviewed across 16 centres in Asia and Europe (AEGIS survey). Participants provided clinical data including bloating and pain intensity, IBS-SSS, QoL, and psychosocial questionnaires (GAD7, PHQ9, PHQ15). The analysis was divided into two groups: an Asian cohort (6 centres) and a non-Asian cohort including 8 European centres plus 1 Australian and 1 Israeli centre. Data were analysed using SPSS, employing Mann–Whitney U tests for continuous variables and chi-square tests for categorical variables.

Results: Across 315 IBS patients, subtype distribution, age, BMI, and sex were similar between Asian and Western cohorts. IBS-D was the most common subtype in both regions, followed by IBS-C in Asia and IBS-M in the West. Education and working status differed significantly, and postprandial IBS symptoms were reported by 35.2% of the cohort, yet showed no regional differences. Total IBS-SSS scores did not differ between Asian and Western patients, yet Asian patients reported significantly lower abdominal pain intensity, higher PAGI-SYM lower GI discomfort scores, fewer pain days, but greater impact on daily life. Conversely, Western patients showed slightly higher bloating severity. Satisfaction with bowel function also differed modestly. Psychological scores were comparable across regions. Asian patients showed slightly higher depression, somatisation, and anxiety scores than Western patients, but none of these differences reached statistical significance.

Conclusions: Regional differences in IBS symptom profiles were evident despite similar overall severity. Asian patients reported less pain but greater daily-life impact, while Western patients showed higher bloating severity. Scores for psychological comorbidity (anxiety, depression and extraintestinal symptom reporting) were similar. These findings highlight culturally influenced symptom patterns that may inform more tailored, region-specific IBS management.

-N11-

BURDEN OF INVESTIGATIONS IN PATIENTS WITH IRRITABLE BOWEL SYNDROME
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Introduction: With an estimated prevalence of 4% according to Rome IV criteria, irritable bowel syndrome (IBS) is frequently diagnosed by gastroenterologists. In the absence of alarm features, European and Belgian guidelines favour a positive diagnosis, recommending only limited non-invasive testing. Nevertheless, the Belgian investigation-focused financing system encourages healthcare professionals to order additional examinations, such as a colonoscopy.

Aim: The aim of this study was to retrospectively assess the frequency of tests performed on patients diagnosed with IBS before visiting the outpatient clinic, as well as additional testing performed after the first visit.

Methods: The study population will consist of all patients diagnosed with irritable bowel syndrome at the Department of Gastroenterology and Hepatology of UZ Brussel between the 1st of May 2022 and the 1st of May 2024. This preliminary analysis presents data from 117 out of 778 identified patients, 167 patients were excluded.

Results: At this stage, data from mainly men (n = 83) were analysed. Most patients had diarrhoea-predominant IBS (n = 46), 30 patients had IBS-C (constipation-predominant), 15 had IBS-mixed, three had IBS-undefined. Fifty patients exhibited no alarm symptoms on presentation, 47 had only one alarm symptom, and respectively 18 and two patients had two or three alarm symptoms. Age over 45 years (n = 32), a family history of colon cancer, IBD or coeliac disease (n = 23) and unintended weight loss (n = 12) were the most commonly mentioned alarm symptoms. Only two patients underwent no testing. In the vast majority (n = 102) blood testing was ordered, with serological testing for coeliac disease in 81 patient. Stool tests were obtained in 65 patients, including faecal calprotectin in 53. Endoscopy was ordered in 76 patients: colonoscopy in 57 and gastroscopy in 53 patients. In total, 61 patients underwent medical imaging; 33 had an ultrasound and 31 had a CT scan. Carbohydrate malabsorption was ordered for 22 patients. Even in the absence of alarm features, in 46% (n = 23) of patients endoscopic investigations were performed, while 40% (n = 20) underwent imaging studies.

Conclusions: Almost all patients IBS undergo non-invasive testing. However, in contrast to existing national recommendations, endoscopic and radiological investigations are frequently ordered in these patients, despite the absence of alarm features. A critical appraisal of referral for invasive testing is required to minimise the associated risk for the patient, and to reduced healthcare costs.

THE EFFECT OF LIRAGLUTIDE ON MMC ACTIVITY, HUNGER RATINGS AND AD LIBITUM FOOD INTAKE IN HEALTHY VOLUNTEERS. S. Kuperus (1), E. Ruilova Sosoranga (1), W. Verbeure (1), S. Willekens (1), H. Geysen (1), I. Depoortere (1), J. Tack (1) / [1] Translational Research Centre for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, TARGID.

Introduction: The worldwide increase in obesity prevalence is a major public health concern. For some individuals with obesity, lifestyle interventions may be insufficient to achieve meaningful weight loss. Recently, glucagon-like peptide (GLP-1) analogues have gained substantial prominence within the pharmaceutical field. Liraglutide is a once-daily GLP-1 analogue. Intravenous GLP-1 has been shown to markedly suppress the migrating motor complexes (MMCs) in healthy volunteers. MMCs play an important role in the regulation of hunger, particularly through phase III contractions that coincide with pre-prandial hunger pangs. Beyond reducing overall food intake, liraglutide has been shown to shift dietary choices toward lower-energy-dense foods, thereby contributing to improved energy balance. Understanding these effects is particularly relevant, as the potential influence of GLP-1 based therapy on MMC activity and its implications for hunger regulation remain largely unexplored.

Aim: To evaluate the effects of liraglutide on MMC activity, hunger ratings and ad libitum food intake in healthy volunteers.

Methods: In this double-blind, randomized, placebo-controlled cross-over study, 14 healthy volunteers (BMI between 18 and 25 kg/m²) received subcutaneous injections of liraglutide (0.6 mg) or placebo (saline) for five consecutive days. High-resolution antroduodenal manometry was performed on the 4th day of a treatment period for 5 hours following a 12-hour overnight fast. On the fifth day of a treatment period, participants consumed an ad libitum buffet 5 hours after receiving a standardized breakfast. Subjective gastrointestinal symptoms and appetite were assessed using Visual Analogue Scales (VAS).

Results: The number of MMCs, as measured in 10 participants, was lower during liraglutide treatment compared to placebo, (0.9 vs. 1.5 in the antrum and 0.6 vs. 1.3 in the duodenum for liraglutide and placebo, respectively), although statistical significance was not reached with this sample size. Liraglutide showed a consistent trend toward lower total energy intake during the buffet meal (852 ± 104 kcal vs. 1010 ± 119 kcal with placebo) and modestly reduced consumption of energy-dense macronutrients, including fat (41 ± 6 g vs. 49 ± 6 g) and carbohydrates (103 ± 12 g vs. 115 ± 13 g). Small shifts in food choice were observed, with a slight increase in fruit intake (22.7% ± 4% → 25.6% ± 5%), but changes did not reach statistical significance. In the fasted state, hunger sensations did not differ between placebo and liraglutide throughout a 5-hour period (condition $P = 0.71$; interaction $P = 0.20$). Prospective food intake tended to vary significantly over time depending on the treatment ($P = 0.09$). A significant condition-by-time interaction ($P = 0.03$) indicated that liraglutide modulated satiety differently compared to placebo during the 5-hour fasting period. Interestingly, before a standardized breakfast was served, satiety sensations tended to be lower over a thirty-minute fasting period ($P = 0.07$). Conversely, liraglutide significantly delayed the return of hunger after breakfast consumption, compared to placebo ($P = 0.02$) and altered prospective food intake scores differently over time in the postprandial period ($P = 0.04$). Fasting blood glucose levels did not differ at baseline between placebo and liraglutide and remained stable over 5 hours of fasting in both groups. However, as expected, a significant condition-by-time interaction effect was found in the postprandial state ($P = 0.02$).

Conclusions: The number of MMCs was lower during liraglutide treatment compared to placebo, although this difference did not reach statistical significance, likely due to the lower sample size attributable to technical complications. Additionally, while liraglutide did not significantly reduce energy intake, it demonstrated consistent directional effects toward lower calories consumption, altered appetite-related sensations over time and lowered postprandial blood glucose responses. These findings suggest that liraglutide subtly influences eating behaviour, subjective appetite, postprandial glucose dynamics, and gastrointestinal motility.

BELGIAN GROUP FOR DIGESTIVE ONCOLOGY (BGDO)

-O01-

LIVER TRANSPLANTATION FOR UNRESECTABLE COLORECTAL LIVER METASTASES: POOLED REAL-WORLD DATA FROM ALL BELGIAN LIVER TRANSPLANT CENTRES. G. Rasschaert (1), M. Vandermeulen (2), M. Van den Eynde (3), H. Eker (4), T. Vandamme (5), C. Loly (6), B. Bracke (7), X. Verhelst (8), J. Verbeek (9), H. Van Vlierberghe (8), V. Labille (6), F. Van Herpe (1), B. Op de Beeck (10), V. Lucidi (11), C. Verslype (1), K. Geboes (12), T. Chapelle (7), G. Dahlqvist (13), J. Pirenne (14), O. Detry (2), L. Coubeau (15) / [1] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Gastrointestinal Oncology Department, University Hospitals Leuven, Leuven, Belgium, [2] CHU de Liège, Liège, Belgium, Abdominal and Transplant Surgery Department, University Hospital Liège, Liège, Belgium, [3] UCLouvain, Cliniques universitaires Saint-Luc, Belgium, Oncology Department, Cliniques Universitaires Saint-Luc, Bruxelles, Belgium, [4] University Hospital Ghent (UZ Gent), Gent, Belgium, General and Hepatopancreatobiliary Surgery Department, University Hospital Gent, Gent, Belgium, [5] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Oncology Department, University Hospital Antwerpen, Antwerpen, Belgium, [6] CHU de Liège, Liège, Belgium, Gastroenterology Department, University Hospital Liège, Liège, Belgium, [7] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Hepatopancreatobiliary and Transplant Surgery Department, University Hospital Antwerpen, Antwerpen, Belgium, [8] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology Department, Hepatology Division, University Hospital Gent, Gent, Belgium, [9] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Gastroenterology and Hepatology Department, University Hospitals Leuven, Leuven, Belgium, [10] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Radiology Department, University Hospital Antwerpen, Antwerpen, Belgium, [11] Hôpital Universitaire de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Brussels, Belgium, Hepatopancreatobiliary & liver transplant surgery department, Hôpital Universitaire de Bruxelles, Bruxelles, Belgium, [12] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology Department, Gastrointestinal Oncology Division, University Hospital Gent, Gent, Belgium, [13] UCLouvain, Cliniques universitaires Saint-Luc, Belgium, Gastroenterology and Hepatology Department, Cliniques Universitaires Saint-Luc, Bruxelles, Belgium, [14] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Abdominal Transplant Surgery Department, University Hospitals Leuven, Leuven, Belgium, [15] UCLouvain, Cliniques universitaires Saint-Luc, Belgium, Abdominal Surgery Department, Cliniques Universitaires Saint-Luc, Bruxelles, Belgium.

Introduction: Liver transplantation (LTx) for unresectable colorectal liver metastases (uCLM) has recently gained renewed interest, particularly following the 2024 publication of the TransMet trial, which provided prospective, randomized evidence supporting the oncologic potential of this strategy in highly selected patients. This has led to an increased demand of LTx for uCLM in all Belgian transplant centres, albeit in the absence of a nationally harmonized protocol during this period of early clinical adoption. Recognizing the growing number of individual cases and the heterogeneity in selection criteria, we sought to retrospectively collect and analyse all Belgian cases of LTx performed for uCLM to date. Especially taken into account that the total number of patients transplanted for this indication in TransMet (38), SECA-I (21) and SECA-II (15) remains modest. Although these initial Belgian cases were not performed under a uniform protocol, this national, multi-centre, retrospective cohort offers a timely and relevant snapshot of clinical practice just prior to the launch of a nationally agreed-upon framework for the indication of LTx in uCLM.

Aim: Assess and consolidate current real-world data to inform future practice and contribute to the broader international discourse on this emerging indication.

Methods: This multicentre retrospective study included all LTx cases performed for uCLM across the six accredited Belgian LTx centres. Patient selection at each centre followed local protocols, which varied and often differed from the exact TransMet protocol. However in all cases, CLM were classified as permanently unresectable and there was no prior history of extrahepatic disease.

Results: Between June 20, 2016 and August 31, 2025, 29 patients underwent LTx for uCLM in Belgium. Patients had a median age of 56 years (IQR 50 – 61) and 20 (69%) of 29 patients were male and 9 (31%) were female. 23 (79%) of 29 primary colorectal tumours were left sided, 4 (14%) were right sided, 2 (7%) had a rectal tumour. 27 (93%) of 29 patients had synchronous CLM and 2 (7%) had metachronous

metastatic disease. All tumours were pMMR/MSS, 2 (7%) of tumours had a KRAS mutation, 2 (7%) had a BRAF mutation and 25 (86%) were RAS/BRAF wild type. At liver transplantation patients received a median of 22 chemotherapy cycles (IQR 16–28) in up to two lines of chemotherapy. During first-line chemotherapy, 18 (62%) had received doublet chemotherapy and 11 (38%) had received triplet regimens; 27 (93%) of 29 had targeted therapy. Serious adverse events occurred in 18 (62%) of 29 patients who underwent liver transplantation. Three patients had an acute rejection, no patient was retransplanted, one patient died from intraoperative haemorrhage. Median follow-up was 20.5 months (IQR 7.0–35.3). 11 (38%) of transplanted patients had a recurrence, in 8 (73%) the site was pulmonary, in 3 (27%) it was peritoneal. The median time to recurrence was 6.3 months (IQR 5.3–6.7). 2-year progression-free survival (PFS) was 35.7% (95% CI 12.8–64.9) among 14 patients eligible for analysis; 1-year PFS was 47.6% (95% CI 25.7–70.2) among 21 patients. 2-year overall survival (OS) was 53.3% (95% CI 43.3–74.1) among 15 patients eligible for analysis; 1-year OS was 68.2% (95% CI 45.6–85.8) among 22 patients. The two BRAF-mutated patients in this cohort have follow-ups of 36 and 110 months, respectively, and are alive without relapse.

Conclusions: LTx for uCLM is feasible in Belgian practice, with encouraging short-term outcomes despite heterogeneous selection criteria and relatively short follow-up. However the recurrence rate was high despite the limited timeframe, though notably, no hepatic recurrences were observed. Our results suggest BRAF status alone (among other mutations) should not exclude patients from LTx; disease control and behaviour might be more relevant. These retrospective findings should be interpreted cautiously but support further uptake of LTx in clinical practice, while emphasizing the importance of a standardized national protocol to optimize patient selection and improve long-term outcomes.

-002-

BELGIAN PROTOCOL FOR INDICATION AND SELECTION OF PATIENTS WITH UNRESECTABLE COLORECTAL CANCER LIVER METASTASES ELIGIBLE FOR LIVER TRANSPLANTATION. G. Rasschaert (1), M. Vandermeulen (2), M. Van den Eynde (3), H. Eker (4), T. Vandamme (5), B. Bracke (6), V. Xavier (7), J. Verbeek (8), H. Van Vlierberghe (7), H. Topal (9), V. Labille (10), D. Monbaliu (11), B. Op de Beeck (12), T. Gustot (13), M. Sainz Barriga (11), F. Sclafani (14), V. Vandecaveye (15), T. Vanwolleghem (16), C. Amicone (10), V. Lucidi (17), C. Verslype (18), T. Chapelle (6), K. Geboes (19), G. Dahlqvist (20), J. Pirenne (11), O. Detry (2), L. Coubeau (21) / [1] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Gastrointestinal Oncology Department, University Hospitals Leuven, Leuven, Belgium, [2] CHU de Liège, Liège, Belgium, Abdominal and Transplant Surgery Department, University Hospital Liège, Liège, Belgium, [3] UCLouvain, Cliniques universitaires Saint-Luc, Belgium, Oncology Department, Cliniques Universitaires Saint-Luc, Bruxelles, Belgium, [4] University Hospital Ghent (UZ Gent), Gent, Belgium, General and Hepatopancreatobiliary Surgery Department, University Hospital Gent, Gent, Belgium, [5] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Oncology Department, University Hospital Antwerpen, Antwerpen, Belgium, [6] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Hepatopancreatobiliary and Transplant Surgery Department, University Hospital Antwerpen, Antwerpen, Belgium, [7] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology Department, Hepatology Division, University Hospital Gent, Gent, Belgium, [8] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Gastroenterology and Hepatology Department, University Hospitals Leuven, Leuven, Belgium, [9] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Abdominal Surgery Department, University Hospitals Leuven, Leuven, Belgium, [10] CHU de Liège, Liège, Belgium, Gastroenterology Department, University Hospital Liège, Liège, Belgium, [11] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Abdominal Transplant Surgery Department, University Hospitals Leuven, Leuven, Belgium, [12] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Radiology Department, University Hospital Antwerpen, Antwerpen, Belgium, [13] Hôpital Universitaire de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Brussels, Belgium, Gastroenterology and Hepatology Department, Hôpital Universitaire de Bruxelles, Bruxelles, Belgium, [14] Hôpital Universitaire de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Brussels, Belgium, Gastrointestinal Oncology Department, Hôpital Universitaire de Bruxelles, Bruxelles, Belgium, [15] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Radiology Department, University Hospitals Leuven, Leuven, Belgium, [16] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology and Hepatology Department, University Hospital Antwerpen, Antwerpen, Belgium, [17] Hôpital Universitaire de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Brussels,

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Introduction: Colorectal cancer (CRC) is common in Western countries, about 50% of patients develop liver metastases (CLM). While local CLM therapies can achieve 5-year survival up to 60%, most patients eventually become unresectable (uCLM) and have poor outcomes with systemic treatment alone. Prospective studies, including SECA I and II and the TransMet trial, showed that in carefully selected patients, liver transplantation (LTx) can achieve survival outcomes comparable to standard LTx indications.

Aim: The aim of this work was to develop a harmonized national consensus protocol for the indication and selection of uCLM patients eligible for LTx.

Methods: Under the coordination of the Belgian Liver & Intestine Advisory Committee (Be-LIAC), all six Belgian transplant centres delegated a transplant surgeon, an oncologist and an hepatologist to a working group that performed a literature review and drafted preliminary criteria. Three successive national meetings and a structured voting refined these criteria in the current protocol.

Results: Consensus was reached on inclusion and exclusion criteria for LTx in uCLM. Two key conditions are liver-only disease and technically uCLM. Strict requirements include a six months disease stability or response on systemic therapy and an obligatory eight-week treatment holiday. Absolute CEA levels and specific somatic mutations are not excluded. An independent central auditing committee was established.

Conclusions: A harmonized national protocol for LTx in uCLM has been established, ensuring consistent patient selection across all Belgian centres. Stricter criteria and an independent auditing committee aim to optimize outcomes while maintaining ethical allocation of donor organs.

-O03-

TARGETING THE LIVER: INSIGHTS FROM A TERTIARY CENTRE ON POST-OPERATIVE HEPATIC ARTERIAL OXALIPLATIN FOR METASTATIC COLORECTAL CANCER. K. Sarti (1), M. Gelli (2), P. Beunon (3), B. Bonnet (3), L. Tselikas (3), G. Camilleri (4), E. Fernandez-de-Sevilla (2), C. Smolenschi (4), M. Valéry (4), A. Fuerea (4), D. Malka (5), T. Pudlarz (4), A. Tarabay (4), A. Hollebecque (4), M. Ducreux (4), V. Boige (4), A. Boileve (4) / [1] CHU-UCL-Namur site Godinne, Yvoir, Belgium, Gastroenterology, [2] Institut Gustave Roussy, Villejuif, France, Surgery, [3] Institut Gustave Roussy, Villejuif, France, interventional radiology, [4] Institut Gustave Roussy, Villejuif, France, medical oncology, [5] Institut Mutualiste Montsouris Paris, Paris, France, medical oncology.

Introduction: As the liver is the most common site of metastasis in colorectal cancer (CRC), and metastatic recurrence frequently occurs after resection of colorectal liver metastases (CRLM), hepatic arterial infusion chemotherapy (HAIC) has emerged as a promising treatment approach.

Aim: To investigate the feasibility, safety, and efficacy of postoperative HAIC with oxaliplatin following curative-intent resection of CRLM.

Methods: A retrospective analysis was conducted on all patients with resected CRLM who received postoperative HAIC with oxaliplatin between 2008 and 2022 at a tertiary cancer centre. The primary study endpoint were disease-free-survival (DFS) and overall survival (OS).

Results: Overall, 119 patients (median age, 56 years; synchronous metastatic disease, 82%) received postoperative HAIC with oxaliplatin after complete resection of their CRLM (median number of metastases resected, 7). They received a median number of 6 HAIC cycles (range, 1–12), mostly combined with intravenous chemotherapy with 5-fluorouracil/leucovorin (n=118, 99%) and irinotecan (n=41, 34%). The median DFS was 10.2 months (95%CI, 9–12.4; 12 month DFS rate, 42%). The median OS reached 55.5 months (95% CI, 50.0–86.6; 5-year OS rate, 46%). Grade 3–4 toxicities occurred in 45% of patients (neutropenia, 38%; peripheral neuropathy, 9%); 54% of patients experienced pain (mostly mild to moderate) during oxaliplatin infusion. HAI catheter-related complications included extrahepatic perfusion (30%) and catheter occlusion (11%).

Conclusions: HAIC with oxaliplatin is an effective, safe and feasible treatment option after resection/ablation of CRLM. These findings support the therapeutic relevance of postoperative HAIC in liver-limited metastatic CRC.

-004-

COLORECTAL CANCER METASTASES HARBOUR DISTINCT MICROBIAL SIGNATURE SHARED WITH THE PRIMARY TUMOURS. J. Deneft (1), P. Stevens (2), L. Coubeau (2), E. Benidovskaya (3), R. Tito (4), G. Bravo-Ruiseco Sanchez (4), P. Baldin (5), V. Lacroix (2), D. Leonard (6), R. Bachmann (2), L. Craciun (7), S. Gofflot (8), F. George (9), F. Sandras (10), J. Sadones (11), M. Buys (12), S. Aydin (13), P. Cani (14), M. Derrien (4), V. Lloréns-Rico (15), J. Raes (4), M. Van den Eynde (2) / [1] UCLouvain, Cliniques universitaires Saint-Luc, Belgium, Institut de Recherche Expérimentale et Clinique (IREC), Department of Medical Oncology, Institut Roi Albert II - Centre for Microbiology - Department of Microbiology, Immunology and Transplantation (Laboratory of Molecular Bacteriology), [2] UCLouvain, Cliniques universitaires Saint-Luc, Belgium, Institut de Recherche Expérimentale et Clinique (IREC), Department of Medical Oncology, Institut Roi Albert II, [3] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, Institut de Recherche Expérimentale et Clinique (IREC), [4] VIB-KU Leuven, Leuven, Belgium, Centre for Microbiology - Department of Microbiology, Immunology and Transplantation (Laboratory of Molecular Bacteriology), [5] UCLouvain, Cliniques universitaires Saint-Luc, Belgium, Department of Medical Oncology, Institut Roi Albert II, Department of Pathology, [6] UCLouvain, Cliniques universitaires Saint-Luc, Belgium, Institut de Recherche Expérimentale et Clinique (IREC), Department of Medical Oncology, Institut Roi Albert II, [7] Hôpital Universitaire de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Brussels, Belgium, Department of Pathology and Biobank, Institut Jules Bordet, [8] CHU de Liège, Liège, Belgium, Department of Pathology and Biobank, [9] Centre Hospitalier Universitaire Mont-Godinne, Belgium, Department of Pathology and Biobank, [10] HUB Hôpital Erasme, Brussels, Belgium, Department of Pathology and Biobank, [11] UZ Brussel, Brussels, Belgium, Department of Pathology and Tumourbank, [12] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Department of Pathology and Tumourbank, [13] UCLouvain, Cliniques universitaires Saint-Luc, Belgium, Department of Medical Oncology, Institut Roi Albert II, Department of Pathology, [14] Université Catholique de Louvain (UCLouvain), Brussels, Belgium, Metabolism and Nutrition Research Group, Louvain Drug Research Institute (LDRI), Walloon Excellence in Life Sciences and BIOTEchnology (WELBIO Department), [15] Centro de Investigación Príncipe Felipe (CIPF), Valencia, Spain, Systems Biology of Host-Microbiome Interactions Lab.

Introduction: The role of intra-tumoural microbiome in cancer development and progression is increasingly reported. Yet, its study is challenging due to low-microbial biomass and contamination risk. Very few studies report bacterial dissemination to distant metastatic sites that could alter tumoural behaviour and microenvironment.

Aim: Our objective is to characterize tumour-resident bacteria in colorectal cancer (CRC) metastases (MT), matched primary tumours (PT), and in a control group of non-CRC tumours (liver PT and non-CRC liver MT).

Methods: We investigated the presence of tumour-resident bacteria in metastatic CRC (mCRC) using 16S rRNA gene sequencing on frozen surgical samples from CRC PT and MT from different sites (liver, lung, peritoneum, ovary and brain) and paired-normal adjacent tissue (NAT). We analysed 615 mCRC samples (147 patients) categorized into four distinct cohorts, each designed for a specific purpose: large-scale profiling, reproducibility, collection and preservation method assessment, and validation under contamination-controlled conditions. As the liver was the most frequent metastatic site, we also included non-CRC liver samples (liver PT and breast cancer liver metastases (BCLM)) for comparison and disease specificity assessment. To ensure the accuracy of our results, we collected and processed the samples following strict contamination-aware protocols with many negative controls and developed a bioinformatic decontamination pipeline to monitor environmental and cross-sample bacterial contamination. We further developed a validation approach to detect the presence of bacterial DNA in highly colonized samples by Fluorescent In Situ Hybridization (FISH) using probes targeting specific genera.

Results: By 16S rRNA gene sequencing and through our stringent decontamination approach, we identified key genera specific to mCRC. The most predominant and significantly abundant taxa across CRC PT and MT included *Fusobacterium*, *Bacteroides*, *Phocaeicola* and members of *Clostridia* class, detected across four metastatic organs. Comparative analyses with non-CRC samples revealed minimal overlap between CRC liver MT, liver PT and BCLM, suggesting that bacterial composition is more disease-specific than organ-specific. Focusing our analyses on intra-patient sharing, we showed that 26 mCRC patients exhibited a

sharing of genera between CRC MT and their corresponding PT. *Fusobacterium* and *Bacteroides* were the most frequently shared genera, identified across three metastatic organs (liver, lung, peritoneum), both synchronously and metachronously. Using FISH with specific probes, we confirmed bacterial presence in CRC PT and MT samples, reinforcing the sequencing-based findings.

Conclusions: Our analyses revealed a consistent and distinct microbial signature in mCRC. Shared microbial taxa between PT and MT support potential bacterial dissemination during cancer progression. Mechanistic studies are now needed to elucidate their role within the tumour microenvironment to understand how they shape the local immune response and influence disease outcome.

-O05-

AEROSOLIZED INTRAPERITONEAL CHEMOTHERAPY FOR PERITONEAL METASTASES FROM GI CANCER. A. Hamdany (1), W. Ceelen (1), W. Willaert (2) / [1] Ghent University Hospital, Gent, Belgium, Belgium, Gastrointestinal surgery, [2] Ghent University Hospital, Ghent, Belgium, Gastrointestinal surgery.

Introduction: Peritoneal metastases (PM) have a dismal prognosis. Laparoscopic aerosolized intraperitoneal chemotherapy (known as PIPAC) may improve outcomes and palliate symptoms in this hard to treat patient group.

Aim: To report tolerability, toxicity, and treatment response in patients treated with PIPAC for PM from GI cancer.

Methods: Data were collected from patients treated with PIPAC between September 2015 and November 2025. Variables included demographics, number of PIPACs, treatment response (radiology, peritoneal cancer index (PCI), tumour markers, histopathology of peritoneal samples), and postoperative complications graded with the Clavien-Dindo classification. Overall survival was analysed from time of PM diagnosis.

Results: In total, 261 patients (M: 51.3%) with a mean age of 59.7 years (range 16-96) underwent 730 PIPACs. A median of three PIPACs (range 1-16). The majority of patients (63.6%) received concurrent systemic chemotherapy. Most had a gastric (25.7%), colorectal (21.5%) or pancreatic adenocarcinoma (13.8%). Postoperative complications occurred in 22.1% of patients, mostly grade I-II (87.5%), five grade III, and two grade IV events. Postoperative abdominal pain was the most common complication. Radiological assessment in 129 patients showed stable disease, regression, or progressive PM in 62%, 7.8%, and 30.2%, respectively. The PCI score in 152 patients after two PIPACs decreased, remained stable, or increased in 24.3%, 41.4%, and 34.2%, respectively. Tumour markers (available in 56 patients) decreased in 46.4% and increased in 48.2% of patients. Histological analysis showed regression, mixed response, or absent response in 26.7%, 31.8%, and 41.5% of patients, respectively. Median overall survival from time of PM diagnosis was 17.0 months (95% CI 13.4-20.6) in gastric adenocarcinoma (N=38), 19.0 months (95% CI 11.0-27.0) in colorectal adenocarcinoma (N=26), and 25.0 months (95% CI 17.8-32.2) in pancreatic adenocarcinoma patients (N=24).

Conclusions: Aerosolized intraperitoneal chemotherapy is well tolerated and safe in patients with PM, and can be combined with parallel systemic treatment. Repeated PIPAC treatments result in demonstrable anticancer activity and promising survival. These results warrant formal exploration of PIPAC treatment in randomized comparative trials.

-O06-

PRELIMINARY EFFICACY AND SAFETY OUTCOMES OF IVOSIDENIB IN PATIENTS WITH IDH1 MUTATED CHOLANGIOCARCINOMA (MIDH1 CCA): INITIAL RESULTS FROM THE BELGIAN COHORT OF THE PROVIDHE STUDY. K. Geboes (1), A. Demols (2), I. Borbath (3), V. D'Cruz (4), S. Ribeiro (4), J. Dekervel (5), G. Rasschaert (5), F. Van Herpe (6), J. Van Laethem (2), A. De Cuyper (7), B. Devos (8), C. Verslype (5) / [1] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology, Division of Digestive Oncology, Ghent University Hospital, Ghent, Belgium, [2] Department of Gastroenterology and GI oncology, Hôpital Erasme, Hôpital Universitaire de Bruxelles, Université Libre de Bruxelles, Brussels, Belgium, Brussels, Belgium, Department of Gastroenterology and GI Oncology, [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Department of Hepato-gastroenterology and digestive oncology, [4] Ghent University Hospital, Ghent, Belgium, Gent, Belgium, Department of Gastroenterology, Division of Digestive Oncology, [5] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Department of Gastroenterology/Digestive Oncology, [6] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Department of Gastroenterology/Digestive Oncology, [7] Cliniques universitaires Saint-Luc, Brussels, Belgium, Brussels, Belgium, Department of Hepato-gastroenterology and digestive oncology, [8] Servier Benelux, Anderlecht, Belgium, Medical affairs.

Introduction: Ivosidenib (IVO) demonstrated efficacy as oral inhibitor of the protein encoded by the mutant isocitrate dehydrogenase 1 (mIDH1) gene in patients (pts) with cholangiocarcinoma (CCA) in the phase 3 ClarIDHy study.

Aim: ProVIDHe, the ongoing phase 3b study, aims to collect additional safety and efficacy data to confirm the benefit of IVO in pts with mIDH1 CCA in real-world setting in 15 countries. Here we report preliminary safety and efficacy results of the Belgian cohort.

Methods: Adult pts with locally advanced or metastatic mIDH1 CCA who had received at least 1 prior line of systemic treatment were included in this study. Pts received 500mg IVO orally once daily and continued treatment as long as there was clinical benefit without unacceptable toxicity. Primary study endpoint is safety, secondary endpoints are efficacy (Progression Free Survival, PFS; Overall Survival, OS; Partial Response, PR; Stable Disease, SD; Duration of Response, DoR), quality of life, and medical resources utilization. Time-to-event endpoints in the presence of censoring are estimated using Kaplan-Meier (KM) methodology with PFS and OS estimates and 95% CIs.

Results: On 17 January 2025, 23 pts from Belgium were included in the Full Analysis Set with a median follow-up to determine overall survival of 7 mo (95% CI; 4.4, 10.4). Median age was 67 years with 39.1% of pts under 65 years. The median number of prior systemic regimens was 1, mainly gemcitabine-cisplatin with immunotherapy (73.9%). Median treatment duration with IVO was 3.7 months (mo); 8.7% of pts achieved PR. Disease control rate (PR + SD) is achieved in 60.9% of pts. Median PFS was 5.6mo (95% CI; 2.1, NE), 6 mo PFS rate was 46.1% and 6 mo OS rate was 77.6%. Most common grade 3 or higher related Treatment Emergent Adverse Event (TEAE) was prolonged QT interval in 2 pts (8.7%). Serious TEAE considered IVO related was rash in 1 patient (4.3%).

Conclusions: This analysis of the Belgian cohort of the ProVIDHe study suggests that the efficacy and safety profile of IVO aligns with that observed in the ClarIDHy trial, reinforcing the therapeutic potential of IVO, also after first line treatment including immunotherapy. The study is still ongoing and future analyses will provide long-term follow-up.

-007-

SAFIR ABC10: TARGETED MAINTENANCE THERAPY VERSUS FIRST-LINE STANDARD OF CARE IN ADVANCED BILIARY CANCER. I. Borbath (1), J. Bridgewater (2), A. Lopez (3), T. Vandamme (4), D. Couch (5), M. Jimenez (5), A. Mc Leer (6), K. Zwaenepoel (7), J. Wong (8), S. Machmahon (9), M. Muller (10), M. Jary (11), A. Hollebecque (12), J. Dekervel (13), A. Demols (14), A. Arora (15), R. Begum (16), L. Dewever (17), J. Edeline (18), D. Malka (19) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Gastro-entérologie, [2] University College London Hospital, London, UK, United Kingdom, Oncology, [3] Cancer Research UK & UCL Cancer Trials Centre, University College London, London, United Kingdom, Oncology, [4] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology, [5] Unicancer, Paris, France, Research And Development Department, [6] Centre Léon Bérard, Lyon, France, Biologie des Cancers, [7] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Pathology, [8] Institut Curie, Saint Cloud, France, Pathology, [9] Royal Marsden Hospital, London, United Kingdom, Clinical Genomics, [10] CHU Nancy, Nancy, France, Oncology, [11] CHU Clermont - Ferrand, France, Medical Oncology, [12] Institut Gustave Roussy, Villejuif, France, Oncologie, [13] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Digestive Oncology, [14] Hôpitaux Universitaires de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Belgium, Gastroenterology and Digestive Oncology, [15] Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom, Oncology, [16] Cancer Research UK & UCL Cancer Trials Centre, University College London, London, United Kingdom, Cancer Trials Centre, [17] BGDO - Belgian Group of Digestive Oncology, Zaventem, Belgium, Cancer trials, [18] Centre Eugène Marquis, Rennes, France, Oncologie médicale, [19] Institut Mutualiste Montsouris Paris, Paris, France, Gastroenterology.

Introduction: The first-line standard of care (1L-SoC) for advanced biliary tract cancers (ABC), a heterogeneous group of malignancies of the bile ducts and gallbladder, is cisplatin and gemcitabine combined with anti-PD-(L)1. In second line and beyond, molecular targeted therapies (MTT) are the preferred options for the 30-50% of ABC that harbor actionable molecular alterations. To date, no randomized data exist for MTT in the first-line setting.

Aim: SAFIR-ABC10 is an international, randomized, Phase 3 umbrella trial comparing the efficacy of on-target MTT maintenance after 12-week 1L-SoC versus continued 1L-SoC using a predefined, scalable, portfolio of target/MTT combinations with a firm level of evidence of potential efficacy according to the

ESMO Scale for Clinical Actionability of molecular Targets (ESCAT I or II): IDH1 mutations/ivosidenib, FGFR2/futibatinib, HER2 amplification/zanidatamab, HER2 mutations/neratinib-trastuzumab, and BRAF V600 mutations/encorafenib-binimetinib. Primary endpoint is progression-free survival (PFS). Secondary endpoints include overall survival, toxicity, tumour response and quality of life. Exploratory endpoints include predictive factors of response and mechanisms of primary and acquired resistance.

Methods: In an initial screening phase, a tumour molecular profile will be obtained from 800 patients (pts) with ABC. Genomic profiling is offered within the National Healthcare System in France and UK. In Belgium, it is performed specifically for the trial, at UZA. Circulating tumour DNA profiling is also performed pre- and during treatment. An international molecular tumour board (MTB) provides a treatment orientation for each pt. Pts with disease control (response or stable disease) after 12-week 1L-SoC, whose tumour harbors ESCAT I-II alteration, are randomized (2:1) to receive on-target MTT maintenance or continued 1L-SoC. A total of 159 pts will be sufficient to detect a HR of 0.60 for PFS, with 80% power and 2-sided 5% significance level.

Results: Recruitment began in June 2024. As of 30.11.2025, 57 centres have been activated in Belgium (1), France and UK, and 493 pts have been enrolled and screened, of which 359 (72%) have been evaluated by the MTB. The screened population has a mean age of 63 years (19-92), 52% are women. Cancer subtype is available for 411 patients, of whom 253 (61.5%) are intrahepatic cholangiocarcinoma, 78 (19%) are extrahepatic and 80 (19.5%) are gallbladder cancers. Among the 359 patients discussed at the MTB, 248 (69%) had no MTT target; 35 (10%) had FGFR2 fusions, 32 (9%) IDH1 mutations, 24 (7%) HER2 amplifications (20 pts) or mutations (4 pts); 8 (2%) BRAF mutations; furthermore 5 patients have MSI-High status. Fifty-five patients have been randomized. Their mean age is 59 y.o. (29-79), 54% are women. Cancer subtype consists of 46 (83.5%) intrahepatic cholangiocarcinoma, 7 (13%) extrahepatic and 2 (3.5%) gallbladder cancers. They were randomized to SoC (18 pts, 33%), Futibatinib (13 pts, 24%), Ivosidenib (13 pts, 24%), Zanidatamab (5 pts, 9%), Neratinib-Trastuzumab (1 pt, 2%), Binimetinib-Encorafenib (4 pts, 8%).

Conclusions: SAFIR ABC10 is recruiting at a high pace, with > 50% of the target sample screened, and 34.5% (55/159 pts) randomized. Targetable alterations were found in 104 pts (29%) of patients (including 1% MSI-High pts), of which 55 are randomized. Belgium centres are currently open(ing).

-O08-

CLINICAL OUTCOMES IN CURATIVELY RESECTED DMMR/MSI-H COLON CANCER: RETROSPECTIVE ANALYSIS OF A MULTICENTRIC COHORT. S. De Meulder (1), M. De Wulf (2), H. Decaestecker (3), L. Decaestecker (4), F. Dedeurwaerdere (5), E. Devolder (6), S. Gryspeerdt (7), P. Pattyn (8), R. Dresen (9), X. Sagaert (10), E. Van Cutsem (6), F. Van Herpe (6), J. Decaestecker (11), A. Wolthuis (12), A. D'Hoore (12), J. Dekervel (6) / [1] AZ Delta, Belgium, Gastroenterology, [2] Ghent University Hospital, Gent, Belgium, Belgium, Medicine, [3] KU Leuven, Leuven, Belgium, Medicine, [4] KU Leuven, Leuven, Belgium, Bioscience engineering, [5] AZ Delta, Belgium, Pathology, [6] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [7] AZ Delta, Belgium, Radiology, [8] AZ Delta, Belgium, Abdominal surgery, [9] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Radiology, [10] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Pathology, [11] AZ Delta, Belgium, Gastroenterology, [12] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Abdominal surgery.

Introduction: Deficient mismatch repair (dMMR) colon cancer accounts for approximately 15% of localised cases and, despite favourable long term survival after curative resection, disease recurrence remains a key concern. Recent trials reported a 3-year disease-free survival of about 80% (1, 2) after primary surgery with or without adjuvant chemotherapy. In the NICHE-2 trial, with the addition of ipilimumab and nivolumab in the neoadjuvant setting, no relapses were observed at three years (3). The same immunotherapy doublet provides a 3-year overall survival rate of 81% in the metastatic setting (4). **Aim:** To describe the relapse risk and survival outcomes in patients with curatively resected dMMR/MSI-H colon cancer across two Belgian centres, and to contextualise these real world data against emerging trial evidence.

Methods: We conducted a retrospective multicentric cohort study including patients with dMMR/MSI H colon cancer who underwent a curative resection at UZ Leuven and AZ Delta between January 1, 2013 and December 31, 2020. Patients with synchronous metastases, microsatellite stable (MSS) tumours or insufficient follow up data (<3 years) were excluded. Clinical characteristics, adjuvant therapy, relapse incidence and survival outcomes were analysed.

Results: A total of 183 patients with curatively resected dMMR/MSI H colon cancer were included. Median age was 72 years (range 24–95). Of the total cohort, stage I accounted for 6.0%, stage II for 72.1% and stage III for 21.9%. Adjuvant chemotherapy was administered in 52 patients (28.4%). Median follow-up time was 61 months (5.1 years). Relapse occurred in 10 patients (5.5%), comprising 4 patients with stage II disease and 6 patients with stage III disease. The 3-year DFS was 96.6% (95% CI: 93.9-99.3%). Of those relapsing, 7 received subsequent immunotherapy, yet 3 of those ultimately succumbed to the disease. The 5-year disease specific mortality was 1.1% (95% CI: 0.0-2.7%), while the 5-year overall mortality was 5.7% (95% CI: 3.5-7.9%). Based on cross-trial comparisons, 30 patients need to be treated with neoadjuvant ipilimumab/nivolumab to avoid one recurrence and 91 patients to avoid one cancer-specific death at 3 years of follow-up.

Conclusions: In this multicentric Belgian cohort of curatively resected dMMR/MSI H colon cancer, recurrence rates were lower than anticipated. In addition, most patients died from other non-related causes. A trade-off between neoadjuvant ipilimumab/nivolumab versus primary surgery and salvage treatment with the same regimen should be discussed based on the high numbers needed to treat to avoid one recurrence and the non-trivial immunotherapy related toxicity (5).

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-O09-

COMPARATIVE ANALYSIS OF CEA LEVELS AT DIAGNOSIS AND RECURRENCE IN PATIENTS WITH COLON CANCER: A MULTICENTRIC RETROSPECTIVE STUDY. E. Devolder (1), S. De Meulder (2), L. Decaestecker (3), I. Bovré (3), H. Decaestecker (3), P. Pattyn (4), M. De Wulf (3), T. Tollens (5), F. Van Herpe (6), S. Gryspeerdt (7), E. Van Cutsem (6), X. Sagaert (8), F. Dedeurwaerdere (9), R. Dresen (8), J. Decaestecker (2), A. Wolthuis (10), P. Cuyle (11), A. D’Hoore (10), J. Dekervel (6) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [2] AZ Delta, Belgium, Digestive oncology, [3] KU Leuven, Leuven, Belgium /, [4] AZ Delta, Belgium, Department of Surgery, [5] KU Leuven, Leuven, Belgium, Department of Surgery, [6] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Digestive oncology, [7] AZ Delta, Belgium, Radiology Department, [8] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Imaging & Pathology, [9] AZ Delta, Belgium, Pathology, [10] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Surgery, [11] Imelda Hospital, Bonheiden, Belgium, Digestive oncology.

Introduction: Colon cancer is a major health burden. Even with complete surgical resection, colon cancer carries a substantial risk of local or distant recurrence. Carcinoembryonic antigen (CEA) is widely used in postoperative surveillance. Rising CEA levels may indicate recurrence, often before clinical or radiologic signs appear. However, approximately 70% of colorectal tumours do not produce or secrete significant amounts of CEA into the bloodstream. As a result, the applicability of this assay may be limited.

Aim: This multicentric retrospective study aimed to evaluate the diagnostic value of serial CEA monitoring after curative resection for non-metastatic colon cancer, including in patients who presented with normal CEA at diagnosis.

Methods: A retrospective analysis was conducted across three Belgian centres (UZ Leuven, AZ Delta Roeselare, Imelda Hospital Bonheiden). Patients with non-metastatic colon cancer who underwent curative-intent surgery between 2013 and 2020 and had at least three years of follow-up were included. Clinical, pathological and demographic data were extracted from electronic health records. CEA levels at diagnosis and at confirmed recurrence were analysed. Elevated CEA was defined as >5 ng/mL. Disease recurrence was established based on either radiologic evidence (ultrasound or CT imaging) or confirmation through histopathological analysis.

Results: From 4,095 screened patients, 695 individuals were included in this cohort. Tumours were predominantly moderately differentiated (75%) and left-sided (62%). A total of 139 cases (20%) were diagnosed in stage I, 264 cases (39%) in stage II and 282 cases (41%) in stage III. All tumours in this cohort had proficient mismatch repair (pMMR) status. Almost half of the patients received adjuvant treatment (43%), and among those treated, the majority received 6 months of therapy (84%). 91 patients (13%) developed recurrence during follow-up. At diagnosis, 514 patients (74%) had normal CEA values, while 181 (26%) showed elevated levels. CEA was elevated at recurrence in 64% of relapsing patients. Notably, among patients who had a normal CEA at diagnosis, 38% exhibited elevated CEA at recurrence. Conversely, 28% of recurrent cases showed no CEA elevation at any time point.

Conclusions: This multicentric analysis demonstrates that CEA rises in a substantial proportion of patients at the time of recurrence, including those who were CEA-negative at diagnosis.

-O10-

GERMLINE MEN1 TESTING PATTERNS IN YOUNG PATIENTS WITH NEUROENDOCRINE TUMOURS: A 12-YEAR RETROSPECTIVE ANALYSIS WITHIN NETWERK, ENETS CENTRE OF EXCELLENCE. L. Mariën* (1), S. Chhajlani* (2), K. Ceulemans (2), M. Leuridan (3), N. Van Daele (3), S. Van Hoegaerden (3), T. Vandamme* (2), K. Janssens* (4) / [1] Universiteit Antwerpen - NETwerk, Antwerp, Belgium, Centre for Medical Genetics, [2] UZA (Universitair Ziekenhuis Antwerpen) - NETwerk, Edegem, Belgium, Medical Oncology, [3] Universiteit Antwerpen / Antwerp University Hospital, WILRIJK (Antwerpen), Belgium, Faculteit Geneeskunde en Gezondheidswetenschappen, [4] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Centrum Medische Genetica.

Introduction: Germline testing in neuroendocrine tumour (NET) patients is inconsistently applied, often guided by clinical judgement due to limited recommendations beyond Multiple Endocrine Neoplasia type 1 (MEN1). Although MEN1 testing guidelines and validated risk nomograms exist, their real-world use and documentation of testing rationale and family history remain unclear. Clarifying current testing patterns and alignment with risk-estimation tools may support a more standardized MEN1 testing approach.

Aim: To evaluate MEN1 germline testing practices and their concordance with nomogram-predicted genetic risk.

Methods: Patients diagnosed with NET before the age of 50 (2016-2024) across NETwerk, a Belgian ENETS Centre of Excellence were retrospectively reviewed. Data included tumour site, testing status, and family history. Germline analyses comprised MEN1 sequencing and, when indicated, extended NET panels. Testing frequency, rationale, and concordance with retrospectively applied nomogram-predicted risk were assessed.

Results: MEN1 germline testing was performed in 43% (n = 40) of 93 patients (53F, 40M; median age 41y) with pancreatic (n = 63), pulmonary (n = 16), or gastric (n = 14) NET. Family history was recorded in 54 (58%), with 13 positive. MEN1 (likely) pathogenic variants were detected in 26 patients, including 17 identified before NET diagnosis. One pulmonary NET patient carried a germline BRCA2 mutation (c.6275_6276delTT). After excluding known MEN1 carriers (n=17), the nomogram was retrospectively applied to 76 patients. Nine were classified as (very) high risk (risk score >10% or > 50%), but only six were tested. Among 67 low (<5%, n=27) or intermediate (5-10%, n=40) risk patients, 17 were tested, identifying three MEN1 and one BRCA2 carrier. These findings show under-testing of high-risk and apparent over-testing of low-risk cases, with pathogenic variants nevertheless detected in the latter, suggesting the nomogram alone may not capture all genetic susceptibility.

Conclusions: Germline MEN1 testing in NET patients <50y was inconsistent and often discordant with nomogram-predicted risk. Several untested patients met high-risk thresholds, revealing a testing gap, while variants were also found in low-risk groups, showing risk-based selection is insufficient. Integrating nomogram-based risk with pragmatic, guideline-supported clinical evaluation within multidisciplinary workflows is key for systematic genetic screening.

PHASE II RAINSPOT: A MULTICENTRIC OPEN LABEL TRIAL OF ZOLBETUXIMAB-PACLITAXEL-RAMUCIRUMAB IN SECOND LINE SETTING FOR CLDN18.2 POSITIVE GASTRO-ESOPHAGEAL ADENOCARCINOMA: TRIAL IN PROGRESS. F. Van Herpe (1), A. Bucalau (2), E. Callebout (3), M. Van den Eynde (4), T. Vandamme (5), P. Vandecandelaere (6), M. De Wit (1), K. Dumon (1), G. Chiritescu (1), G. Rasschaert (1), S. Vanstraelen (7), J. Dekervel (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology, [2] Institut Jules Bordet, Brussels, Belgium, Oncology, [3] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology, [4] UCL Saint-Luc, Brussels, Belgium, Oncology, [5] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Oncology, [6] AZ Delta, Belgium, Gastroenterology, [7] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Thoracic surgery.

Introduction: Claudin 18.2 (CLDN18.2) has recently emerged as an important therapeutic biomarker in gastro-oesophageal adenocarcinoma, with phase III trials (SPOTLIGHT/GLOW) demonstrating significant overall survival (OS) and progression-free survival (PFS) benefits from adding zolbetuximab, an anti-Claudin 18.2 antibody, to first-line chemotherapy. However, In Belgium patients with CLDN18.2-positive tumours currently do not have access to zolbetuximab as there is no reimbursement. Outside of Belgium some patients progressing after first-line therapy remain without access to zolbetuximab, when first-line treatment involves immunotherapy.

Aim: The RAINSPOT trial aims to evaluate the efficacy and safety of adding zolbetuximab to standard second-line paclitaxel–ramucirumab in patients with CLDN18.2-positive advanced gastro-oesophageal adenocarcinoma previously untreated with anti-CLDN18.2 agents. Secondly we will assess the potential loss of CLDN18.2 expression following first-line progression and explore the efficacy of Zolbetuximab in patients with lost-CLDN18.2 expression and maintained CLDN18.2 expression respectively.

Methods: RAINSPOT is a national, multicentre, phase II, open-label study comprising one prospective single-arm cohort and a matched retrospective cohort across six Belgian centres (UZ Leuven, UZ Antwerp, UZ Gent, AZ Delta Roeselare, HU Brussels and UC Louvain) In the prospective cohort we aim to include 100 patients in a recruitment periode of 24 months. In this cohort eligible patients are ≥ 18 years with metastatic or locally advanced gastro-oesophageal adenocarcinoma, ECOG PS 0–1, who progressed after one prior line of systemic therapy (chemotherapy $\pm$ immunotherapy). Tumours must be CLDN18.2-positive, defined as $\geq 75\%$ moderate-to-strong membranous staining using the Ventana CLDN18 [43-14A] RxDx assay in the initial diagnostic tissue. A fresh biopsy after first-line progression is obtained when feasible to assess changes in CLDN18.2 expression and its impact of Zolbetuximab efficacy. Patients will receive Zolbetuximab IV 800 mg/m² loading dose (Cycle 1 Day 1), then 400 mg/m² every 2 weeks, Paclitaxel 80 mg/m² weekly $\times$ 3 every 28 days and Ramucirumab 8 mg/kg every 2 weeks. The recent Delphi consensus will be followed for the management of treatment related emesis and nausea. Treatment continues until progression or unacceptable toxicity. Safety is monitored continuously for 90 days after the last zolbetuximab dose. HRQoL is assessed every 4 weeks (EORTC QLQ-C30 and QLQ-OG25). In the retrospective cohort patients are eligible if treated between January 2021 and December 2023 with paclitaxel–ramucirumab in second line, for whom archived tissue is re-evaluated for CLDN18.2 expression. Only patients with CLDN18.2 positivity at baseline will be eligible. Propensity score matching (1:1; tolerated SMD ≤ 0.05) is performed using age, sex, tumour location, previous gastrectomy, peritoneal metastases, and study centre.

Results: As this is an ongoing trial, no efficacy or safety results are yet available. Enrollment is planned for 24 months, with an additional 24 months of follow-up after the last zolbetuximab dose. Planned analyses include comparisons of OS and PFS between the prospective and matched retrospective cohorts, descriptive toxicity profiling, objective response rate (ORR) and HRQoL.

Conclusions: RAINSPOT is the first study investigating zolbetuximab combined with paclitaxel–ramucirumab in the second-line treatment of CLDN18.2-positive gastro-oesophageal adenocarcinoma. This trial addresses a significant therapeutic gap for patients who did not receive zolbetuximab in first line. By integrating a carefully matched real-world comparator cohort, RAINSPOT aims to generate robust evidence regarding survival outcomes and treatment tolerability together with QoL. The results are expected to inform optimal sequencing of targeted and immunotherapeutic strategies in advanced gastro-oesophageal cancer.

THE 1000-NEN-GENOME PROJECT: AN INTERNATIONAL WHOLE GENOME SEQUENCING INITIATIVE TO UNCOVER GERMLINE PREDISPOSITION FOR NEUROENDOCRINE TUMOURS. K. Janssens (1), L. Mariën (2), S. Chhajlani (3), K. Op de Beeck (4), G. Van Camp (4), T. Vandamme (5)

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Introduction: Germline predisposition in neuroendocrine tumours (NET) remains poorly understood. Familial clustering has been observed in select subgroups, and only eight inherited cancer predisposition syndromes have been identified to date, suggesting additional, undiscovered predispositions. Moreover, the true prevalence of pathogenic germline variants in NET is uncertain, with estimates ranging from 4.5% to 45%. Existing genome-wide association studies (GWAS) are limited by small sample sizes, restricted coverage, and heterogeneity. Clarifying the germline contribution is crucial, as targeted screening and genetic counselling of high-risk individuals could enable earlier diagnosis and curative interventions.

Aim: To determine the prevalence and spectrum of (likely) pathogenic germline variants in patients with NET through whole genome sequencing (WGS), and to further explore polygenic risk modelling.

Methods: A large cohort of over 1,000 patients with pancreatic, small intestinal, or pulmonary NETs (stage I–IV) without known hereditary syndromes is being assembled across 17 study sites in five countries (Belgium, The Netherlands, France, Italy and Australia). Through the FORCE and BE-FORCE initiatives (NCT06541080) approximately two-thirds of cases have been collected, with additional cohorts under recruitment. Pseudonymized clinicopathological data are entered into a centralized database, and germline DNA from buffy coats undergoes WGS. Analyses will include (i) monogenic variants in known NET- or cancer-associated genes and hypothesis-free variant discovery; (ii) digenic variant prediction via the VarCoPP algorithm, a first-of-its-kind approach in NET; and (iii) GWAS and polygenic risk modelling using PLINK. For the latter, large WGS control cohorts are being sought. In addition, a dedicated NET Variant Curation Board is being assembled to systematically review and report clinically relevant germline findings.

Results: Recruitment and data harmonization across sites are ongoing. DNA extraction and sequencing of the first batch (n = 64) are scheduled for January 2026. The bioinformatic analysis pipeline has been established and will be internally validated soon.

Conclusions: This project will provide the most comprehensive insight to date into germline alterations in NET, enabling earlier detection and interventions. First results are expected in 2026. The study is funded by Stichting Tegen Kanker and has received ethical committee approval.

-O13-

ENHANCING CLINICAL TRIAL ACCESS FOR NEN PATIENTS THROUGH A CROSS-SITE ‘FLYING’ STUDY COORDINATOR WITHIN NETWORK - ENETS CENTRE OF EXCELLENCE. C. De Weerd (1), S. Chhajlani (1), S. Raats (1), L. Mariën (1), O. Islam (1), L. Verbruggen (1), J. De Loose (1), I. Maurissen (2), M. Ulenaers (3), W. Lybaert (4), T. Vandamme (1) / [1] UZA (Universitair Ziekenhuis Antwerpen) - NETwerk, Edegem, Belgium, Oncology, [2] ZAS - NETwerk, Antwerp, Belgium, Gastroenterology, [3] AZ Rivierenland - NETwerk, Bornem, Belgium, Gastroenterology, [4] VITAZ - NETwerk, Sint-Niklaas, Belgium, Oncology.

Introduction: NETwerk - ENETS Centre of Excellence (CoE) is a collaborative network of seven hospitals, with the University of Antwerp as academic partner. Within this multidisciplinary framework, experts work together to optimize the diagnosis, treatment and care of patients with neuroendocrine neoplasms (NEN). Several clinical trials are conducted within NETwerk with the largest proportion of patients included within Antwerp University Hospital (UZA), as limited research capacity in affiliated regional hospitals hinders patient inclusion and clinical trial accessibility. To address this gap and strengthen cross-site collaboration, the concept of a ‘flying’ study coordinator was introduced in 2023 to provide flexible, on-site research activity across NETwerk hospitals, thereby facilitating patient recruitment and improving research integration and patient outcomes.

Aim: This project aims to assess the impact and added value of the cross-institutional ‘flying’ study coordinator within NETwerk through quantitative and qualitative evaluation of clinical research performance before and after the role’s implementation.

Methods: To evaluate the quantitative impact on patient recruitment, pre- and post-intervention inclusion rates (before implementation of the ‘flying’ study coordinator in 2023 versus after two years of operation) were

extracted from local databases and calculated for each participating regional hospital, including VITAZ, AZ Rivierenland, and Ziekenhuis aan de Stroom (ZAS). The perceived added value of this cross-site coordination model for local research activity is assessed by distributing tailored questionnaires to a diverse group of healthcare professionals across these hospitals. The survey addresses multiple domains, including operational efficiency, investigator engagement, workload distribution, patient benefit, scientific output, trial accessibility, and interinstitutional collaboration. Questionnaire dissemination and data analysis will be completed in Q1 2026 and results will be presented at the BWGE 2026 Conference.

Results: During the two years following the implementation of the ‘flying’ study coordinator (2023–2025), patient recruitment increased by 58% in VITAZ (from 97 to 153 inclusions), by 625% in AZ Rivierenland (from 4 to 29), and by 58% in ZAS (from 31 to 49). The model also enabled the initiation of two new multicentric international clinical trials across three additional NETwerk hospitals beyond UZA and facilitated inclusion in phase I investigational medicinal product studies in NEN within UZA. These activities strengthened inter-hospital collaboration and knowledge exchange, ultimately enhancing clinical research capacity and care quality.

Conclusions: This initiative of a cross-site ‘flying’ study coordinator demonstrates a pragmatic and scalable model to overcome structural and logistical barriers to clinical trial participation across multiple sites, bridging the gap between regional and academic hospitals within NETwerk. By centralizing coordination and delivering highly specialized on-site research support for NEN patients, the ‘flying’ study coordinator effectively reinforces research capacity which ultimately improves patient outcomes. This concept may be extrapolated to other rare diseases or collaborative research settings requiring specialized cross-site expertise.

-O14-

FROM A COMPLETE RESPONDER TO DUAL IMMUNE-CHECKPOINT INHIBITION TO NOVEL IMMUNOTHERAPY STRATEGIES IN UNRESECTABLE HEPATOCELLULAR CARCINOMA. F. Peeters (1), O. Bricard (2), G. Philips (2), S. Cappuyns (3), C. Verslype (3), D. Lambrechts (2), J. Dekervel (3) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Digestive oncologie, [2] VIB-KU Leuven, Leuven, Belgium, Centre for Cancer Biology, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Digestive Oncologie.

Introduction: Hepatocellular carcinoma (HCC) will become a leading cause of cancer mortality and outcomes for patients with unresectable disease remain poor. Although dual immune checkpoint inhibition (ICI) with anti-PDL1 and anti-CTLA4 monoclonal antibodies can induce durable, or even complete, responses in a minority of patients, most experience primary or acquired resistance. Moreover, upon disease progression there are few treatment options with many patients being too frail for second-line regimens. Therefore, there is a critical unmet need for innovative new treatment strategies that improve patient outcomes without introducing severe side-effects.

Aim: By using translational insights from tissue and blood samples of a patient who achieved a complete pathological response to dual ICI, we aim to generate scientific rationale for novel immunotherapy strategies in unresectable HCC, ultimately resulting in a phase I clinical trial with individualized mRNA vaccination.

Methods: We present a case of a 68-year old male patient with radiographic evidence of a large, hypervascular hepatic mass and an elevated alpha-fetoprotein (AFP) of 116088.00 µg/L. The patient exhibited a remarkable erythrocytosis, with a haemoglobin of 19.0g/dL and a hematocrit of 59.2% caused by a markedly increased plasma erythropoietin level. There was no biochemical or radiological evidence of underlying liver cirrhosis. Laparoscopic biopsy of the mass confirmed the diagnosis of HCC. Given the insufficient targeting for selective internal radiation therapy (SIRT) and the high AFP, the multidisciplinary tumour board advised to start with dual ICI with anti-PDL1 and anti-CTLA4 monoclonal antibodies. After only four cycles of systemic therapy, the patient exhibited a normalization of AFP, haemoglobin, hematocrit and erythropoietin levels. Follow-up magnetic resonance imaging (MRI) showed a significant therapy response with a reduction of the maximal tumour diameter and near-complete resolution of diffusion restriction. Surgical resection of the residual hepatic mass was performed and histopathological examination revealed no evidence of viable tumour cells. Tissue and blood samples from before and after administration of systemic treatment, were used to identify tumoural antigens using our in-house developed in vitro tumoural antigen identification technique, named TWISTAR.

Results: In this patient with initially unresectable HCC, who achieved a complete pathological response to dual ICI treatment, we identified 10 tumoural antigens. Notably, several of these antigens were also detected in tumours from other patients with HCC and across other tumour types, both in our HCC cohort and in publicly

available datasets. Given the growing scientific evidence that mRNA cancer vaccines and ICI therapy can act synergistically, these findings form the basis for TWISTVAX-01, an academically driven phase I clinical trial in patients with unresectable HCC that will be conducted in UZ Leuven. TWISTVAX-01 is designed to evaluate the safety, feasibility and immunogenicity of an individualized mRNA cancer vaccine targeting patient-specific tumour antigens, combined with dual ICI treatment. Each mRNA vaccine is tailored to the patient's antigenic landscape, identified using our TWISTAR antigen identification platform. This personalized approach is expected to generate a more potent and clinically meaningful antitumour immune response, while its synergy with ICI may overcome primary or acquired resistance to immunotherapy. Moreover, given the favorable safety profile of mRNA vaccines, this strategy is expected to add minimal toxicity, which is especially important for patients with unresectable HCC, who frequently have underlying liver disease and are vulnerable to treatment-related toxicities.

Conclusions: This unique case of an initially unresectable, erythropoietin-producing HCC, achieving a complete pathological response to dual ICI, highlights the potential of ICI in unresectable HCC. By identifying immunological-relevant tumour antigens, we provide a rationale for developing personalized immunotherapy strategies, soon moving forward in the phase I TWISTVAX-01 clinical trial.

-O15-

UNCOVERING THE HIDDEN FAT: MYOSTEATOSIS AS A NOVEL PROGNOSTIC MARKER IN PANCREATIC ADENOCARCINOMA. M. Ayari (1), S. Ben Azouz (2), A. Chehaider (2), H. Douggui (2), T. Jomni (2) / [1] Internal Security Forces Hospital La Marsa, Tunis, Tunisia, Hepato-gastroenterology, [2] Internal Security Forces Hospital La Marsa, Tunis, Tunisia, Hepato-gastroenterology.

Introduction: Pancreatic cancer remains a highly lethal malignancy, with a significant mortality rate largely due to late-stage diagnosis, early metastatic potential and poor response to conventional therapies. Considering these challenges, the identification of novel prognostic factors is essential to improve outcomes. Radiologic sarcopenia has been recognized in multiple studies as an independent prognostic factor in pancreatic cancer. In contrast, myosteatosi s, characterized by fatty infiltration within skeletal muscle tissue, remains underexplored, and its prognostic value in pancreatic cancer has not been sufficiently investigated.

Aim: The aim of our study was to investigate the relationship between pre-therapeutic myosteatosi s and survival outcomes in pancreatic cancer.

Methods: We conducted a retrospective, single-centre study, including patients diagnosed with pancreatic adenocarcinoma between 2014 and 2022. We have excluded patients having computed tomography (CT) performed in others centres and not included in our database. Skeletal muscle density of the psoas muscle was measured using axial CT images at the third lumbar vertebra level. On a single axial slice at this level, the right and left psoas muscles were manually segmented using specialized imaging software (Weasis DICOM medical viewer). Once the psoas muscles are delineated, the density was quantified in Hounsfield Units (HU). Based on prior studies, myosteatosi s was defined based on mean skeletal muscle density cutoff values less than 41 HU for patients with body mass index (BMI) under 25 kg/m² and less than 33 HU for those with a BMI of 25 kg/m² or higher.

Results: A total of 30 patients were included in the study with a mean age of 61 ± 11 years and a sex-ratio F/M of 0.25. The most common tumour location was in the pancreatic head (66.6% of cases). At the time of diagnosis, the tumour was classified as resectable in 11 patients (36%), locally advanced in 10 patients (33%) and metastatic in 9 patients (30%). Regarding treatment, 33.3% of patients underwent surgery and 30% received palliative chemotherapy. The mean psoas muscle attenuation value was 31.84 ± 9.99 HU (range 13.5-63 HU). The overall incidence of myosteatosi s was 66.7% (N = 20). The mean overall survival was 12 ± 12.75 months. Recurrence-free survival rates at 6 months, 12 months and 36 months were 50%, 36.7% and 25% respectively. In univariate analysis, myosteatosi s was significantly associated with lower albumin level (30.94 ± 5.73 vs 38 ± 4.13, p = 0.002) and advanced stage pancreatic cancer (p=0.003). Myosteatosi s was not associated with diabetes mellitus, smoking, anemia, lymphopenia or CA 19-9 level. In terms of survival, the difference between the two Kaplan-Meier curves of patients with myosteatosi s versus those without was statistically significant (log rank test p=0.007), with a mean survival period of 7.10 ± 10.33 versus 21.80 ± 11.78 months respectively (p=0.002). Myosteatosi s was associated with a two-fold increased risk of mortality (HR = 2.25; 95% CI: 0.267–18.925). When analysing the receiver operating characteristic (ROC) curve, AUC of TPAI in predicting 12 months survival was 0.749 (95% CI: 0.563–0.934, p=0.025).

Conclusions: Pre-therapeutic myosteatosi s was identified in approximately two-thirds of patients with pancreatic adenocarcinoma and was significantly associated with reduced overall survival. These findings

highlight the prognostic value of muscle density, as assessed by CT-derived muscle attenuation, and support its potential role as a valuable prognostic marker for risk stratification and personalized management in pancreatic cancer.

-O16-

PROGNOSTIC VALUE OF THE SKELETAL MUSCLE INDEX AND PSOAS MUSCLE AREA INDEX IN COLORECTAL CANCER: A RETROSPECTIVE COHORT STUDY. M. Ayari (1), W. Khemiri (2), S. Ben Azouz (2), A. Chehaider (2), H. Douggu (2), T. Jomni (2) / [1] Internal Security Forces Hospital La Marsa, Tunis, Tunisia, Hepato-gastroenterology, [2] Internal Security Forces Hospital La Marsa, Tunis, Tunisia, Hepato-gastroenterology.

Introduction: Sarcopenia, defined as a decrease in muscle mass and strength, is emerging as a potential prognostic factor in malignancies. In the literature, radiological sarcopenia has been assessed using the skeletal muscle index (SMI) with a validated threshold.

Aim: This study aimed to investigate the prognostic value of pretherapeutic radiological sarcopenia in Tunisian patients with colorectal cancer (CRC) and to assess the validity of the psoas muscle area index (TPAI) in evaluating sarcopenia.

Methods: A retrospective study including patients diagnosed with CRC from 2014 to 2022 was conducted. Sarcopenia was assessed on a cross-sectional CT scan at the level of the third lumbar vertebra by calculating SMI and TPAI. A SMI lower than 52.4 cm²/m² and 38.5 cm²/m² for male and female gender respectively defined sarcopenia. TPAI index was calculated using the formula: $TPAI = (\text{Left Psoas Area [mm}^2\text{]} + \text{Right Psoas Area [mm}^2\text{]}) / (\text{Height [m]})^2$.

Results: Eighty-four patients were included with a mean age of 60.6 ± 12.7 years and a M/F sex ratio of 1.89. Sarcopenia according to SMI was observed in 63% of patients, statistically correlated with older age (p=0.004), male gender (p=0.008), lymphopenia (p=0.01), hyperferritinemia (p=0.04), elevated platelet-to-lymphocyte ratio (p=0.01) and carcinoembryonic antigen level (p=0.005). In multivariate study, advanced age (OR=6.67; 95%CI [1.81-24.48]; p=0.004) and male gender (OR=5.59; 95%CI [1.57-19.86]; p=0.008) were independent factors associated with sarcopenia. TPAI was significantly correlated with SMI (Pearson p<0.001; r=0.717 respectively). The TPAI thresholds predicting of sarcopenia were 7.52 cm²/m² and 4.83 cm²/m² for male and female gender respectively. Overall survival was significantly reduced in patients with sarcopenia, with 1-, 3-, and 5-year survival rates of 58%, 37%, and 26% versus 80%, 68%, and 53% (log Rank=0.001). The survival study showed that sarcopenia was an independent factor of mortality (OR=4.43; 95%CI [1.07-18.25]; p=0.04).

Conclusions: Pretherapeutic radiological sarcopenia is a significant prognostic factor in CRC, negatively correlating with survival. We established sex-specific cutoff values in Tunisian patients for TPAI, a reliable predictive marker for sarcopenia and offering a promising alternative to SMI. Systematic assessment of sarcopenia could optimize treatment strategies and improve patient outcomes.

-O17-

TISLELIZUMAB + CHEMOTHERAPY VS PLACEBO + CHEMOTHERAPY AS FIRST-LINE TREATMENT IN GASTRIC/GASTROESOPHAGEAL JUNCTION ADENOCARCINOMA PATIENTS WITH/WITHOUT PERITONEAL OR LIVER METASTASES: A POST HOC ANALYSIS OF RATIONALE-305. M. Qiu (1), H. Luo (1), F. Wang (1), F. Wang (1), M. He (1), S. Xu (2), X. Pan (3), R. Xu (1) / [1] Sun Yat-sen University Cancer Centre State Key Laboratory of Oncology, Guangzhou, China, Medical Oncology, [2] BeOne Medicines, San Carlos, United States, SGPAC-APAC, [3] BeOne Medicines, San Carlos, United States, MA APAC-GC&EC.

Introduction: Gastric cancer patients with peritoneal or liver metastases have poor prognosis, and the efficacy of immunotherapy in these patients remains unclear. The global phase 3 RATIONALE-305 trial (NCT03777657) demonstrated that tislelizumab (TIS) combined with chemotherapy (chemo) could bring survival benefits to first-line (1L) treatment of patients with gastric/gastroesophageal junction adenocarcinoma (GC/GEJC).

Aim: Here, we assessed the efficacy of TIS+chemo vs placebo (PBO)+chemo in patients with/without peritoneal or liver metastases in RATIONALE-305.

Methods: Patients with systemic treatment-naïve GC/GEJC were randomized (1:1) to receive either

TIS+chemo or PBO+chemo. Regression analyses were conducted to explore the associations between peritoneal or liver metastases and OS. Relative treatment effect between tislelizumab and placebo was assessed in each subgroup. The Kaplan-Meier method was used to estimate the median OS, and hazard ratios (HRs) for OS were estimated using Cox proportional hazards models.

Results: Among the 997 randomized patients (TIS+chemo, n=501; PBO+chemo, n=496), 434 (43.5%) had peritoneal metastases (220 in TIS arm; 214 in PBO arm) and 378 (37.9%) had liver metastases (190 in TIS arm; 188 in PBO arm) at baseline. Regression analyses showed peritoneal and liver metastases were significantly associated with shorter OS. Baseline characteristics were balanced between TIS and chemo arms within each subgroup, including PD-L1 expression levels. As of data cut-off on Feb 28, 2024, OS was longer in the TIS arm compared with the PBO arm in patients with peritoneal metastases (HR= 0.78, 95% CI 0.64-0.96) or without (HR = 0.79, 95% CI 0.65-0.95). OS improvement was also observed in patients with liver metastases (HR = 0.77, 95% CI 0.62-0.96) or without (HR = 0.80, 95% CI 0.67-0.95).

Conclusions: This post hoc analysis demonstrated OS improvement with TIS+chemo vs PBO+chemo in GC/GEJC patients with/without peritoneal or liver metastases. To our knowledge, RATIONALE-305 is the first global pivotal study reporting survival benefits with TIS+chemo as 1L treatment for GC/GEJC, irrespective of peritoneal or liver metastases.

-O18-

TISLELIZUMAB + CHEMOTHERAPY (CT) VS PLACEBO + CT IN PATIENTS WITH LOCALLY ADVANCED ESOPHAGEAL SQUAMOUS CELL CARCINOMA: RATIONALE-306 SUBGROUP ANALYSIS. E. Van Cutsem (1), J. Xu (2), E. Raymond (3), R. Hubner (4), H. Yoon (5), K. Kato (6), L. Wyrwicz (7), D. Tougeron (8), S. Park (9), P. Jimenez-Fonseca (10), T. Kojima (11), R. Ishihara (12), A. Avallone (13), R. Pazo-Cid (14), S. Xu (15), S. Yan (16), J. Shi (17), X. Kong (16), F. Lordick (18) / [1] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Division of Digestive Oncology, [2] Fifth Medical Centre, PLA General Hospital, Beijing, China, Medical Oncology, [3] Paris Saint-Joseph Hospital, Paris, France, Medical Oncology, [4] The Christie NHS Foundation Trust, Manchester, United Kingdom, Medical Oncology, [5] Mayo Clinic, Phoenix, United States, Oncology, [6] National Cancer Centre Hospital, Tokyo, Japan, Head and Neck, Esophageal Medical Oncology, [7] Maria Sklodowska-Curie National Cancer Research Institute, Warsaw, Poland, Oncology and Radiology, [8] Poitiers University Hospital, Poitiers, France, Hepato-Gastroenterology, [9] ASAN Medical Centre, University of Ulsan College of Medicine, Ulsan, Korea (the Republic of), Oncology, [10] Central University Hospital of Asturias, Asturias, Spain, Medical Oncology, [11] National Cancer Centre Hospital East, Kashiwa, Japan, Gastrointestinal Oncology, [12] Osaka International Cancer Institute, Osaka, Japan, Gastroenterology, [13] National Cancer Institute IRCCS-G. Pascale Foundation, Naples, Italy, Medical Oncology, [14] Hospital Universitario Miguel Servet, Zaragoza, Spain, Medical Oncology, [15] BeOne Medicines, San Carlos, United States, SGPAP-APAC, [16] BeOne Medicines, San Carlos, United States, Clinical Development, [17] BeOne Medicines, San Carlos, United States, Clinical Biomarker, [18] University of Leipzig Medical Centre, Leipzig, Germany, Medicine.

Introduction: In RATIONALE-306 (NCT03783442), participants (pts) with metastatic/locally advanced (LA) esophageal squamous cell carcinoma (ESCC) were randomized to IV tislelizumab (TIS) 200 mg or placebo (PBO) every 3 weeks plus investigator-chosen chemotherapy (CT; platinum+fluoropyrimidine/paclitaxel) until disease progression, unacceptable toxicity, death, or withdrawal of consent, whichever occurred first. There was improvement in overall survival (OS) in the intent-to-treat (ITT) population (primary endpoint) and a subgroup of pts with PD-L1 Tumour Area Positivity (TAP) score $\geq 10\%$ (secondary endpoint). At the 3-yr follow-up, improvement was sustained in TIS+CT (HR, 0.70; 95% CI: 0.59, 0.83) vs PBO +CT in the ITT population.

Aim: We report a post hoc analysis of RATIONALE-306 in pts with LA ESCC.

Methods: Pts with LA ESCC, with non-metastatic disease and deemed unfit for surgery or definitive chemoradiation, were retrospectively selected and included in this analysis. Efficacy outcomes (OS, progression-free survival [PFS], objective response rate [ORR]) and safety were analysed.

Results: At data cutoff (August 22, 2024), of 649 pts randomized (TIS+CT n=326; PBO+CT n=323), 88 had LA ESCC (TIS+CT n=49; PBO+CT n=39; median age 66.0 yrs; 85.2% male). At a minimum 45-month follow-up, efficacy was improved in pts with LA ESCC compared to the ITT population. The median OS for TIS+CT was 25.6 months (95% CI: 19.4, 36.3) vs 12.3 months (95% CI: 9.0, 21.7) for PBO+CT (HR, 0.49; 95% CI: 0.29, 0.84). Median PFS for TIS+CT was 9.7 months (95% CI: 6.9, 19.6) compared to 6.9 months (95% CI: 4.2, 9.7) for PBO+CT (HR, 0.56; 95% CI: 0.31, 1.01). The ORR was 61.2% (30 of 49

pts) for TIS+CT compared to 38.5% (15 of 39 pts) for PBO+CT. Tolerability in the LA ESCC subgroup was consistent with the ITT population, with no new safety signals. Treatment-related adverse events with TIS+CT vs PBO+CT were 100.0% vs 92.3% (any grade), 59.2% vs 59.0% (grade ≥ 3), and 28.6% vs 20.5% (serious), respectively.

Conclusions: In this subgroup analysis of pts with LA ESCC, first-line TIS+CT showed substantial and clinically meaningful improvements in efficacy, with tolerable safety.

-O19-

THE IMPACT OF EXOGENOUS FACTORS ON BREATH-BASED GASTROESOPHAGEAL CANCER ONCOMETABOLITES: A PHASE I DIAGNOSTIC STUDY. H. Gielen (1), A. Bohyn (2), F. Van Herpe (3), L. Depypere (4), H. Van Veer (4), R. Bisschops (5), J. Dekervel (6), P. Nafteux (1), S. Vanstraelen (1) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Thoracic Surgery, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Biostatistics, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Digestive Oncology, [4] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Thoracic Surgery, [5] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Gastroenterology and Hepatology, [6] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Department of Digestive Oncology.

Introduction: Gastroesophageal cancer remains one of the most prevalent and lethal cancers worldwide. Although upper gastrointestinal endoscopy with biopsy is the current diagnostic gold standard, its limitations as a population-level screening tool are well recognized. Consequently, research efforts are increasingly directed toward novel non-invasive diagnostics, including breath-based biomarkers. Alterations in tumour cellular metabolism generate a distinct oncometabolic signature that can be detected in exhaled alveolar breath using electronic nose (E-nose) technology. While current breath-analysis protocols commonly require extended fasting prior to testing, robust evidence supporting the necessity is lacking.

Aim: This phase I diagnostic study aimed to evaluate the temporal dynamics of breath-derived oncometabolites under various external conditions and quantify both the between-person and within-person variability, using a fully portable E-nose platform.

Methods: The study population included healthy volunteers recruited between May 2025 and October 2025. After a 6-hour fasting period, exhaled alveolar breath samples were collected and analysed using a next-generation metal-oxide E-nose. Each participant underwent three test conditions: eating, drinking or brushing teeth. Following each intervention, breath samples were collected at 30min, 1h, 1.5h, 2h, 3h and 4h. Based on previous work, the five most oncometabolites—highest log-fold change associated with esophageal cancer—were assessed: 2-pentanone, acetone, toluene, butane and 2-propanol. For each oncometabolite, a linear mixed model method was used to assess the temporal changes in oncometabolite concentration (parts per billion, ppb) and to estimate between-person and within-person variance (σ^2). A likelihood ratio test was applied to compare the within-person variance across test conditions. The interclass correlation [ICC] quantified the proportion of total variance attributable to between-person variability, with a high ICC indicating strong within-person consistency over time and a greater contribution of between-person differences.

Results: A total of 33 healthy volunteers completed all three test conditions, including 9 (27%) man and 24 (73%) women, with a median age of 24 years (Range: 19–62). Four participants were current smokers or vapers. Median (IQR) concentration in healthy individuals versus patients with cancer were as follows: 2-pentanone, 3.36 ppb (3.25–3.76) vs 0.11 ppb (0.11–0.12); acetone, 90 ppb (89–91) vs 2,644 ppb (1,790–3,700); toluene, 28 ppb (23–32) vs 454 ppb (268–743); butane, 2.53 ppb (2.42–2.76) vs 0.12 ppb (0.07–0.19); and 2-propanol, 3.59 ppb (3.44–4.18) vs 0.21 ppb (0.09–0.39). For 2-pentanone, the between- and within-person variance over time were 0.364ppb/0.138ppb (eating), 0.402ppb/0.134ppb (drinking) and 0.477ppb/0.153ppb (brushing), corresponding to a ICC of 72.5%, 75.0% and 75.7%, respectively. There was no difference in within-person variance between the test conditions ($p=0.63$). For acetone, the between- and within-person variance over time for acetone were 6.795ppb/3.549ppb (eating), 4.424ppb/3.477ppb (drinking) and 2.772ppb/7.613ppb (brushing), corresponding to a ICC of 65.7%, 56.0% and 26.7%, respectively. Brushing teeth resulted in a greater within-person variance ($p<0.001$). For toluene, the between- and within-person variance over time were 0.000ppb/84.124ppb (eating), 3.426ppb/86.746ppb (drinking) and 3.989ppb/123.442ppb (brushing), corresponding to an ICC of 0.0%, 3.8% and 3.1%, respectively. Brushing teeth resulted in a greater within-person variance ($p=0.008$). For butane, the between- and within-person variance over time were 0.091ppb/0.029ppb (eating), 0.050ppb/0.020ppb (drinking) and 0.054ppb/0.033ppb (brushing), corresponding to a ICC of 75.9%, 70.9% and 62.2%, respectively. Brushing teeth resulted in a

greater within-person variance ($p=0.004$). For 2-propanol, the between- and within-person variance over time were 0.782ppb/0.297ppb (eating), 0.863ppb/0.288ppb (drinking) and 1.023ppb/0.329ppb (brushing), corresponding to a ICC of 72.5%, 75.0% and 75.7%, respectively. There was no difference in within-person variance between the test conditions ($p=0.63$). After locally estimated scatterplot smoothing (LOESS) regression, the variance over time in each test condition remained stable with most effect observed within the first 2h after eating or brushing teeth.

Conclusions: We can conclude that some oncometabolites exhibit low within-person variability, supporting their suitability for long-term monitoring. Exogenous factors appear to influence the within-person variance primarily during the first two hours after exposure. However, given the concentration differences observed between healthy individuals and cancer patients, this short-term exogenous influence is unlikely to meaningfully affect diagnostic performance. While further validation is required, this phase I diagnostic study provides the first evidence that oncometabolites with low within-person variability are preferable for longitudinal assessment and fasting protocols prior to breath analysis may be unnecessary.

-O20-

PRRT-ASSOCIATED NET TO NEC DEDIFFERENTIATION. S. Chhajlani (1), O. Islam (1), A. Florez (2), M. Le Moine (3), J. Kuiper (4), D. Gonzalez Devia (2), A. Driessen (5), I. Geboers (6), K. Kortbeek (3), J. Hofland (4), S. Stroobants (7), T. Vandamme (1) / [1] UZA (Universitair Ziekenhuis Antwerpen) - NETwerk, Edegem, Belgium, Medical Oncology, [2] Fundación Santa Fe de Bogotá, Bogotá, Colombia, Endocrinology, [3] University Hospital of Brussels, Brussels, Belgium, Medical Oncology, [4] Erasmus MC, University Medical Centre Rotterdam, The Netherlands, Internal Medicine, [5] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Pathology, [6] Ziekenhuis Geel, Geel, Belgium, Medical Oncology, [7] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Nuclear Medicine.

Introduction: Peptide receptor radionuclide therapy (PRRT) is a key therapeutic option for advanced well-differentiated (WD) gastroenteropancreatic neuroendocrine tumours (NET). PRRT induces β -radiation-mediated DNA damage, and rarely may contribute to dedifferentiation, leading to aggressive features resembling poorly differentiated (PD) neuroendocrine carcinoma (NEC). This transformation has been reported only in few cases.

Aim: The aim is to describe the clinicopathological, radiological, and molecular features of PRRT-associated NET to NEC dedifferentiation.

Methods: A retrospective, multicentre study was conducted at Antwerp University Hospital, Erasmus Medical Centre, and Fundación Santa Fe de Bogotá, including patients with histologically confirmed post-PRRT dedifferentiation. Clinicopathological, radiological, and molecular data were analysed descriptively.

Results: Five patients (4M, 1F; median age 67y) were included. Primary sites were pancreas ($n=3$), stomach ($n=1$), and small intestine ($n=1$). One patient received prior liver-directed therapy. All patients had SSTR+ lesions at baseline, with 1 showing FDG+/SSTR- mismatch. All patients received 4 cycles of PRRT. Prior treatments included SSA alone ($n=3$) or with chemotherapy ($n=2$; one with an alkylating agent). Following PRRT, all patients developed rapid progressive disease (median time to PD after last cycle: 8.6m). Two had FDG+/SSTR- liver lesions. Pathology showed transformation from WD-NET to PD-NEC ($n=4$; 2 large-cell) or NET with NEC-like features ($n=1$), with increase in Ki-67 index (mean 7.9% pre-PRRT to 77.8% post-PRRT). Molecular alterations in post-PRRT biopsy included RB1 loss ($n=1$), TP53 mutation ($n=1$), ATM mutation ($n=1$), and MSI ($n=1$). One patient had BRCA germline mutation. Outcomes were poor as the mOS was 7.5m ($n=4$), with disease-related mortality in three. One patient remains alive at 14m of follow-up post-dedifferentiation, and is receiving 3rd line immunotherapy.

Conclusions: PRRT-associated dedifferentiation is rare but linked to poor outcomes. Prior liver-directed therapy or alkylating agents may promote aggressive subclones, while PRRT-induced DNA damage may accelerate transformation. Early recognition is critical: FDG-PET can reveal FDG+/SSTR- lesions both pre- and post-PRRT, and pre-PRRT biopsy may help refine risk stratification, while post-PRRT biopsy of progressing lesions should also be performed to confirm transformation and guide treatment. Further research is needed into the tumour biology and predictive markers is needed.

-O21-

CLINICAL AND ONCOLOGICAL IMPACT OF MUSCLE-RELATED PARAMETERS IN OESOPHAGOGASTRIC CANCER. Y. Deswysen (1), E. Danse (2), P. Trefois (2), A. Collard (3), M. Van den

Eynde (4), N. Lanthier (5) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Chirurgie Oeso-Gastrique, Service de Chirurgie et Transplantation Abdominale, Institut Roi Albert II et Laboratoire de gastroentérologie et d'hépatologie, Institut de Recherche Expérimentale et Clinique, UCLouvain, Brussels, Belgium, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service de Radiologie, UCLouvain, Brussels, Belgium, [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Cellule statistique, Clinical Trial Centre, UCLouvain, Brussels, Belgium, [4] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'Oncologie Médicale, Institut Roi Albert II et Service d'Hépto-gastroentérologie, UCLouvain, Brussels, Belgium, [5] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'Hépto-gastroentérologie et Laboratoire de gastroentérologie et d'hépatologie, Institut de Recherche Expérimentale et Clinique, UCLouvain, Brussels, Belgium.

Introduction: Oesophagogastric cancer remains a disease associated with poor survival rates. Skeletal muscle can play a crucial role in this situation and assessing muscle mass and quality can help identify patients with reduced muscle mass (myopenia) and muscle fat infiltration (myosteatosi).

Aim: To assess body composition (muscle mass and muscle quality) in patients with oesophageal or gastric cancer, and to analyse clinical associations and oncological outcomes.

Methods: Patients diagnosed with oesophagogastric cancer between November 2019 and December 2023 were included in this retrospective study. Skeletal muscle index (SMI) and density (SMD) were evaluated via CT scans at the L3 level. Myopenia and myosteatosi were defined according the Martin's criteria: myopenia was defined in men by an SMI $<43 \text{ cm}^2/\text{m}^2$ (BMI <25) or $<53 \text{ cm}^2/\text{m}^2$ (BMI ≥ 25) and in women by an SMI $<41 \text{ cm}^2/\text{m}^2$; myosteatosi was defined by an SMD $<41 \text{ HU}$ (BMI <25) or $<33 \text{ HU}$ (BMI ≥ 25). Clinical parameters (age, BMI, albumin level, CRP – C-reactive protein, NLR – neutrophil-to-lymphocyte ratio and PLR – platelet-to-lymphocyte ratio) and oncological outcomes (OS – overall survival and PFS – progression free survival) were analysed. Univariate and multivariate survival analyses were performed using Cox proportional hazard stepwise regression model.

Results: Among 161 patients (67.1% male, mean age 65.0 ± 12.8 years), 49.1% had oesophageal and 50.9% gastric cancer. Most had adenocarcinoma (64.6%) and 25% had metastases. Mean SMI and SMD were $45.1 \pm 10.5 \text{ cm}^2/\text{m}^2$ and $24.6 \pm 9.6 \text{ HU}$ respectively. Despite a normal median BMI ($25.2 \pm 5.53 \text{ kg}/\text{m}^2$), myopenia and myosteatosi were highly prevalent (62.7% and 87.6%, respectively) based on Martin's criteria. Uni- and multivariate analyses showed that metastases were independently associated with poorer OS (HR 3.28 [95% CI 1.847-5.824], $p < 0.001$) and PFS (HR 3.14 [95%CI 1.896-5.210], $p < 0.001$). SMD and PLR ratio were independent predictors of OS (HR 0.95 [95%CI 0.918-0.992], $p = 0.017$ and HR 1.00 [95%CI 1.001-1.006], $p = 0.005$) and PFS (HR 0.96 [95%CI 0.934-0.998], $p = 0.037$ and HR 1.00 [95%CI 1.001-1.005], $p = 0.002$), whereas CRP was independently associated with OS only (HR 1.00 [95% CI 1.000-1.011], $p = 0.036$). Due to high prevalence of myopia and myosteatosi, and the lack of standardised cut-offs in the literature, muscle mass and density were categorised into tertiles based on their distribution in our study population. The lowest tertile served as the reference group to allow assessment of potential gradient effects with adequate statistical power. Kaplan–Meier survival analysis showed that SMI was significantly associated with poorer OS and PFS: patients with higher muscle mass (upper two tertiles combined) had a higher median OS compared with those in the lowest tertile (NE vs. 18.0 months, HR 0.57 [95%CI:0.36-0.91], $p = 0.0162$). PFS was significantly longer in patients with high muscle mass (25.9 vs. 13.5 months, HR 0.63 [95%CI: 0.42–0.96], $p = 0.0017$). Similarly, SMD was associated with reduced survival. Patients with higher muscle density (less myosteatosi, upper two tertiles combined) had a higher median OS than those in the lowest tertile (NE vs. 20.5 months, HR 0.54 [95%CI: 0.34-0.86]; $p = 0.0089$). No significant difference was observed for PFS based on SMD tertiles. Despite lower muscle density, patients with myosteatosi also had myopenia (42.3 vs $52.6 \text{ cm}^2/\text{m}^2$, $p < 0.0001$).

Conclusions: This study highlights the very high prevalence of myopenia and myosteatosi using Martin's criteria in oesophagogastric cancer patients, even among those with normal BMI. Myopenia and myosteatosi are associated with worse survival outcome of patients. The coexistence of myosteatosi and myopenia suggests that fat infiltration and muscle loss may reflect a common catabolic process in cancer patients. These results support the relevance of body composition assessment for improving risk stratification and informing oncological management. Specific cut-offs for SMI (myopenia) and SMD (myosteatosi) should be proposed for oesophagogastric cancers.

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Introduction: Biliary tract cancers (BTCs) comprise a heterogeneous group of aggressive malignancies with generally poor prognosis. Molecular profiling has become increasingly important for identifying actionable targets, yet real-world data from European populations remain limited.

Aim: This study provides the first comprehensive Belgian real-world cohort study assessing the prevalence, distribution, and prognostic relevance of molecular alterations across BTC subtypes (intrahepatic [iCCA] or extrahepatic [eCCA] cholangiocarcinoma, gallbladder cancer [GBC], or combined hepatocellular-cholangiocarcinoma [cHCC-CCA]).

Methods: The study included all patients with histologically confirmed BTC (CCA, cHCC-CCA, or GBC) who underwent informative molecular testing on tumour tissue as part of routine clinical diagnostics at Antwerp University Hospital (UZA) between May 2016 and December 2024. Demographic, clinical and molecular data were extracted from electronic health records and pathology reports at UZA. Next-generation sequencing, fluorescence in-situ hybridization, and immunohistochemistry were used to characterize genomic alterations. Descriptive statistics summarized demographic data and prevalence of molecular alterations. Fisher's exact test assessed associations for categorical variables. Overall survival (OS) was calculated from the date of diagnosis, and analysed using Kaplan–Meier and Cox regression models. Variables with $p < 0.1$ in univariate analyses were included in multivariate models; $p \leq 0.05$ was considered significant. Statistical analysis was performed using IBM SPSS Statistics 31.

Results: A total of 224 patients with BTC were included in the study (145 patients with iCCA, 22 with eCCA, 30 with CCA NOS (not otherwise specified; i.e. CCA cases without knowledge of further subclassification into iCCA or eCCA), 4 with cHCC-CCA, and 23 with GBC. Median age at diagnosis was 68 years (range 29–89); 120 patients were female and 104 male. Molecular alterations were detected in 59.4% of tumours. MSI-H was significantly associated with male sex. The most frequent alteration was KRAS mutation (20.5%), dominated by G12D (44.2% of KRAS-mutated tumours). Subtype-specific profiles were clearly distinct. iCCA was characterized by IDH1 mutations (17.4%) and FGFR2 fusions (13.9%), both exclusive to this subtype. All IDH1 alterations involved codon R132, most commonly R132C (71%). In eCCA KRAS mutations (42.9%) were the predominant event, while GBC was dominated by ERBB2 amplification (16.7%). Co-alterations were identified in 7.8% of patients and generally involved genes from distinct signaling pathways. IDH1/2 and FGFR2 alterations were mutually exclusive, but IDH1-mutant tumours frequently (7 of 24 mutant tumours) occurred with other secondary hits in complementary oncogenic pathways. Although 37.1% of patients harbored at least one actionable alteration, only 27.3% of eligible individuals with available treatment data received matched targeted therapy, primarily IDH1 or FGFR2 inhibitors (9/14). Among BRAF-mutant tumours, class I (V600E) was most common (41.7%), with class II and III mutations also observed, and dabrafenib/trametinib was administered to one V600E and one class III (D594G) case. In univariate survival analysis, KRAS-mutated tumours were associated with significantly worse OS than wild-type tumours (8.6 vs. 15.4 months; HR 1.75, $p=0.004$), an association that remained irrespective of co-alteration status. IDH1-mutated tumours showed a trend toward improved OS (31.3 (mut) vs. 13.2 months (wt); HR=0.58, $p=0.087$), which persisted but was attenuated after excluding patients treated with ivosidenib. Median OS was similar between IDH1-mutant tumours with and without co-alterations (31.8 vs. 31.3 months). In multivariate analysis including tumour stage, KRAS and IDH1 mutation status, only tumour stage ($p < 0.001$; HR 1.62) and KRAS mutation ($p = 0.012$; HR 1.83) were independently associated with worse OS.

Conclusions: This first Belgian real-world cohort highlights the molecular heterogeneity of BTC and reinforces the clinical relevance of subtype-specific profiling. KRAS mutations emerged as the sole independent marker of poor prognosis, while actionable alterations, particularly IDH1 and FGFR2, were frequent but underutilized in therapeutic decision-making. These findings underscore the need for

systematic molecular testing and improved access to targeted therapies to optimize precision oncology in BTC management.

-O23-

AN OPEN-LABEL, RANDOMIZED, MULTICENTRE, PHASE 3 STUDY OF TRASTUZUMAB DERUXTECAN (T-DXD) + CHEMOTHERAPY (CHEMO) ± PEMBROLIZUMAB (PEMBRO) VERSUS CHEMO + TRASTUZUMAB ± PEMBRO IN FIRST-LINE METASTATIC HER2+ GASTRIC OR GASTROESOPHAGEAL JUNCTION (GEJ) CANCER: DESTINY-GASTRIC05. F. Van Herpe (1), M. Van den Eynde (2), J. Goeminne (3), A. Holvoet (4), A. Bucalau (5), J. Collignon (6) / [1] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Oncology, [2] UCL Saint-Luc, Brussels, Belgium, Gastroenterology, [3] CHU UCL Namur, Yvoir, Belgium, Oncology, [4] AZ Sint-Lucas Brugge, Assebroek/Brugge, Belgium, Gastroenterology, [5] Institut Jules Bordet, Brussels, Belgium, Oncology, [6] CHU Liege, Liège, Belgium, Oncology

Introduction: HER2-positive (HER2+) gastric and gastroesophageal junction (GEJ) cancer remains an area of significant unmet clinical need. Approximately 20% of patients have HER2+ disease. In the KEYNOTE-811 trial, adding pembrolizumab to trastuzumab and chemotherapy improved progression-free survival (PFS) and overall survival (OS) in patients with PD-L1 combined positive score (CPS) ≥ 1 . In the DESTINY-Gastric03 study, first-line regimens combining trastuzumab deruxtecan (T-DXd) with fluoropyrimidines (5-fluorouracil [5-FU] or capecitabine) ± pembrolizumab demonstrated acceptable safety and encouraging efficacy, including in patients with CPS < 1 . These results support further evaluation of a platinum-free, T-DXd-based first-line approach.

Aim: The phase 3 DESTINY-Gastric05 trial aims to assess whether T-DXd combined with chemotherapy ± pembrolizumab improves outcomes compared with standard first-line therapy consisting of trastuzumab plus platinum-based chemotherapy ± pembrolizumab in patients with HER2+ metastatic gastric or GEJ cancer.

Methods: DESTINY-Gastric05 is an open-label, randomized, multicentre phase 3 study. Approximately 576 patients with HER2+ metastatic gastric or GEJ cancer, ≥ 1 measurable lesion (RECIST v1.1), left ventricular ejection fraction $\geq 50\%$, and ECOG performance status 0–1 will be randomized 1:1 to: Arm M1: T-DXd 5.4 mg/kg + 5-FU or capecitabine + pembrolizumab Arm M2: trastuzumab + platinum-based chemotherapy (cisplatin + 5-FU or oxaliplatin + capecitabine) + pembrolizumab The primary endpoint is PFS per blinded independent central review (BICR). The key secondary endpoint is OS. Additional secondary endpoints include overall response rate, duration of response, and time to response (RECIST v1.1, BICR and investigator), as well as safety and tolerability. An exploratory cohort (~150 patients with PD-L1 CPS < 1) will evaluate T-DXd + 5-FU/capecitabine versus trastuzumab + standard chemotherapy.

Results: This is a trial-in-progress; no efficacy or safety results are yet available.

Conclusions: DESTINY-Gastric05 is designed to determine whether a platinum-free, T-DXd-based first-line regimen can improve clinical outcomes for patients with HER2+ metastatic gastric or GEJ cancer compared with current trastuzumab-based standard therapy. The study may broaden therapeutic options across PD-L1 subgroups, including patients with CPS < 1 .

BELGIAN PANCREATIC CLUB (BPC)

-P01-

THERAPEUTIC TARGETING OF SECRETED OSTEOPONTIN ATTENUATES THE FIBROTIC PHENOTYPE IN EXPERIMENTAL CHRONIC PANCREATITIS. E. Gökce (1), L. Devisscher (2), N. Rashidian (3), P. Hindryckx (1) / [1] Ghent University Hospital, Gent, Belgium, Belgium, Department of Gastroenterology and Hepatology, [2] Ghent University, Ghent, Belgium, Department of Basic & Applied Medical Sciences, Gut-Liver Immunopharmacology Unit, Ghent University & Liver Research Centre Ghent, Ghent University Hospital, [3] Ghent University Hospital, Gent, Belgium, Belgium, Department of General and Hepatobiliary Surgery, Liver Transplantation Service.

Introduction: Chronic pancreatitis (CP) is a progressive and irreversible fibro-inflammatory disease of the pancreas, characterized by acinar loss and fibrosis, for which no curative therapy exists. Secreted osteopontin (sOPN) is a matricellular cytokine increasingly recognized as a central mediator of fibrosis across multiple organs, including liver, lung and pancreas. However, its potential as therapeutic target in CP remains unexplored. **Aim:** To investigate the therapeutic potential of targeting secreted osteopontin (sOPN) in chronic pancreatitis, given its increasingly recognized role as a key mediator of fibrosis in multiple organs.

Methods: Mice received six intraperitoneal cerulein injections (50 µg/kg every hour) one day per week, combined with daily ethanol injections (33%, 6×/week) for 3 weeks to induce chronic pancreatitis-like injury. Anti-OPN antibody (200µg, 3×/week) was administered to neutralize secreted OPN. Serum sOPN levels were measured by ELISA. Pancreatic RNA was isolated for qPCR analysis of inflammatory and fibrotic markers, and fibrosis was additionally evaluated histologically using Sirius Red staining. In parallel, serum samples from CP patients (n = 10) were collected and analysed for sOPN levels by ELISA.

Results: Three-weekly injections of cerulein and ethanol induced a consistent CP-like phenotype, characterised by acinar cell loss, inflammatory cell infiltration and early fibrosis. Circulating sOPN levels were significantly higher in mice with CP compared to healthy mice, and significantly decreased upon anti-OPN-Ab treatment. Histological analysis showed a trend towards reduced pancreatic fibrosis, with less collagen deposition on Sirius Red staining. Pancreatic IL-4 and α -SMA mRNA expression showed a trend towards reduced expression in anti-OPN-Ab treated mice (IL-4: 3.87 ± 0.70 vs. 2.79 ± 0.48 , $p > 0.05$; α -SMA: 3.17 ± 0.92 vs. 1.55 ± 0.29 , $p > 0.05$; mean $\pm$ SEM, p-value), while CTGF levels were significantly lower (5.30 ± 0.37 vs. 3.74 ± 0.36 , $p = 0.0179$; mean $\pm$ SEM, p-value), indicating attenuation of the fibrotic phenotype. Consistent with the experimental findings, serum sOPN levels were also increased in CP patients compared to controls.

Conclusions: Blocking secreted OPN reduced serum OPN levels and markers of fibrogenic activation in experimental CP. Together with elevated sOPN levels in patients, these findings support a role for secreted OPN in pancreatic fibrogenesis and identify it as a potential therapeutic target in CP. A six-week experimental model is currently ongoing to further confirm and extend these findings.

-P02-

BURNING MEN: RFA IN RECURRENT PANCREATIC INSULINOMAS AND ITS COMPLICATIONS. D. Coevoet (1), P. Hindryckx (1) / [1] University Hospital Ghent (UZ Gent), Gent, Belgium, Gastroenterology.

Case: A 25-year-old female patient with a multiple endocrine neoplasia type 1 (MEN1) syndrome (previously treated for a prolactinoma and primary hyperparathyroidism) presented with new-onset hyperinsulinemic hypoglycaemic episodes. A CT scan revealed a hypervascular nodular lesion in the pancreatic corpus measuring 18 x 20 mm, highly suggestive of a neuroendocrine tumour. Endoscopic ultrasound confirmed this lesion but also detected 4 smaller lesions, located in the head (N=1, 8mm), the distal body (N=1, 8mm) and the tail (N=2, 10mm and 6mm). EUS-guided sampling confirmed the diagnosis of multifocal NET, with a Ki index <5%. After multidisciplinary discussion and informed consent of the patient, we opted for a multi-session radiofrequency ablation (RFA) of the lesions. In a first procedure, the two largest lesions were treated. Three sessions of RFA (50W) were performed on the largest lesion, and one session (50W) on the largest lesion in the tail. The procedure was complicated by an exudative pancreatitis. After initial resolution of the hypoglycaemic episodes, a relapse was seen 6 months after the initial ablation. An MRI revealed two lesions measuring 7 mm and 8 mm located in the head and tail of the pancreas, suspicious for NET. A DOTATATE scan confirmed elevated DOTATATE uptake in these two lesions and identified a third lesion in the pancreatic corpus (cfr the earlier finding on EUS). A second session RFA was performed on the lesion in the head (8mm, 20W 90

sec) and tail (7mm, only 30 sec because of contacts with the splenic vessels). Again, the patient developed a post-procedural pancreatitis despite preprocedural prophylaxis (NSAID, hyperhydration). Her hypoglycaemic episodes were gone and she was discharged. Three months after the second ablation, the patient reported epigastric pain. A new CT scan revealed dilation of the pancreatic duct in the corpus and tail, along with fibrotic changes around the ablation area in the head. An Endoscopic Retrograde Cholangiopancreatography (ERCP) with retrograde access was unsuccessful. EUS-guided rendezvous was not successful (no passage of the guidewire across the stricture). An EUS-guided gastropancreaticostomy was performed. The procedure was uncomplicated, and the patient was pain-free afterward. Two to three months later, she was readmitted with pancreatitis at 8 weeks of (unplanned) pregnancy. Spontaneous migration of the pancreatic stent was noted, and a new pancreaticogastrostomy was performed. At 18 weeks of pregnancy, she experienced again recurrent hypoglycaemic episodes. In an attempt to avoid invasive treatment during pregnancy, conservative management with dietary modifications and somatostatin analogues was initiated.

Discussion: An insulinoma is a rare functional pancreatic tumour. MEN1 syndrome is associated with multiple insulinomas. These tumours are usually detected at an early stage owing to the prompt onset of clinical manifestations such as hyperinsulinemic hypoglycemia. Surgery remains the standard treatment. However, the multifocal nature of disease in MEN1 often necessitates extensive pancreatic resection, associated with substantial morbidity. Minimally invasive techniques such as EUS-guided RFA have increasingly been applied to small insulinomas, with good long term outcomes. To our knowledge, this is the first reported case of recurrent multifocal insulinomas in a patient with MEN1 treated with RFA. This case underscores the potential of EUS-guided RFA as a parenchyma sparing alternative management in MEN1 patients. However, we were confronted with several procedure related complications. Thus, the benefits and risk of this therapeutic approach should be balanced in a case-by-case manner.

-P03-

EUS-GUIDED INTERNAL DRAINAGE OF A POST-WHIPPLE PANCREATICOJEJUNAL LEAK COMPLICATED BY A CUTANEOUS FISTULIZED COLLECTION: REVERSING THE EXTERNALIZED FISTULOUS FLOW INWARD. S. Aliou (1), J. Navez (2), N. Claeys (2), M. Arvanitakis (1) / [1] HUB Hôpital Erasme, Brussels, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, [2] HUB Hôpital Erasme, Brussels, Belgium, Department of Hepato-Pancreato-Biliary Surgery and Liver Transplantation.

Background: Pancreatic fistulas and anastomotic leaks remain among the most challenging postoperative complications after pancreaticoduodenectomy (Whipple procedure), leading to significant morbidity and prolonged hospitalization. Conventional management relies mainly on percutaneous drainage, nutritional support and use of somatostatin analogues; however, persistent external fistulas can delay recovery and compromise quality of life. In selected cases, endoscopic ultrasound (EUS)-guided internal drainage offers a minimally invasive alternative, promoting closure by redirecting the external output toward an internal controlled route into the gastrointestinal lumen.

Aims: To demonstrate the technical feasibility and clinical efficacy of EUS-guided internal drainage for the management of a postoperative pancreaticojejunal anastomotic leak with cutaneous fistula after Whipple procedure with antrectomy, gastrojejunostomy, pancreaticojejunostomy and hepaticojejunostomy, emphasizing the concept of fistulous flow reversal: redirecting drainage from a persistent external cutaneous route into an internal digestive pathway to promote closure and healing. Additionally, the antrectomy significantly reduces the anatomical window available to safely puncture the collection under EUS guidance, making the procedure technically more challenging.

Methods: A 73-year-old man presented with obstructive jaundice due to a 28 × 14 mm duodenopancreatic groove mass. After inconclusive EUS-FNA, he underwent a pancreaticoduodenectomy (Whipple procedure) on January 2024. Pathology revealed a moderately differentiated pancreatic adenocarcinoma, staged pT2N1R0. The postoperative course was complicated by fever, elevated CRP, and persistent drainage of purulent fluid from a surgical drain. CT imaging revealed a large mesenteric collection (90 × 76 mm) adjacent to the pancreaticojejunal anastomosis, suggesting an anastomotic dehiscence with external fistulization. Despite percutaneous drainage, a persistent output of approximately 50 mL/day remained, indicating a mature external fistula. An EUS-guided internal drainage procedure was performed one month postoperatively with the objective of reversing the flow direction. Using a linear echoendoscope, the collection was identified adjacent to the pancreaticojejunal anastomosis. A puncture was performed through the body of the remaining stomach, next to the gastrojejunostomy, using a 19G Zimmon needle. Contrast injection delineated the

collection and demonstrated its communication with the pancreaticojejunal loop, confirming the diagnosis of anastomotic dehiscence. A guidewire was advanced into the cavity and coiled under fluoroscopic control. A 10 Fr cystotome was used to create a fistulous tract, the first 7 Fr $\times$ 5 cm double pigtail plastic stent was deployed across the tract. Balloon dilation (6 mm) was then performed along the tract to facilitate placement of the second stent. Finally, the second 7 Fr $\times$ 5 cm double pigtail stent was deployed, establishing continuous internal drainage between the collection and the gastric lumen. The procedure was completed without immediate complications.

Results: After the procedure, the external fistula output decreased progressively and stopped within a few days. The patient remained afebrile with progressive clinical improvement. A CT scan performed one day later confirmed the correct intraluminal position of the two stents and showed a marked reduction in the size of the main collection as well as other smaller intra-abdominal collections. Two small residual fistulous tracts were noted along an old surgical drain pathway, without clinical significance. At follow-up imaging two months later, a near-complete regression of the collections was observed, with only a small residual cavity (11 mm) adjacent to the pancreaticojejunal anastomosis. The cutaneous fistula had completely closed. No stent migration or secondary infection occurred. Eight months after the procedure, the patient was asymptomatic, afebrile, and in good general condition, with normal oral intake and weight gain. The stents remained in place and were planned for elective removal. No recurrence of collection or fistula was observed.

Conclusion: This case highlights the value of EUS-guided internal drainage as an effective and minimally invasive approach for the management of postoperative pancreaticojejunal leaks after Whipple procedure. By reversing the direction of flow, from an uncontrolled external cutaneous route to a controlled internal drainage into the digestive lumen, the technique promotes closure of the external tract, accelerates healing, and improves patient comfort while avoiding repeat surgery. EUS-guided internal drainage can be considered in selected patients with accessible collections adjacent to the anastomosis. Proper imaging assessment, controlled access with a cystotome, and secure stent deployment are key to procedural success. This case demonstrates durable clinical success and radiologic resolution, supporting EUS-guided internal drainage as a safe and effective option in the multidisciplinary management of post-Whipple anastomotic leaks.

-P04-

CPA1 VARIANT PATHOGENICITY AND CLINICAL COURSE IN PAEDIATRIC ONSET CHRONIC PANCREATITIS. B. Murari (1), G. Jannone (1), X. Stephenne (1), I. Scheers (1) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Brussels, Belgium, Paediatric Gastroenterology and Hepatology.

Over the past 5 years, we identified 4 children from 3 unrelated families who presented before the age of 3 with recurrent abdominal pain and persistently raised lipase below 3-times the upper limit of normal. Pancreatic magnetic resonance imaging was unremarkable in all cases. Comprehensive evaluation for known causes of pancreatic disease was performed, and each child was found to carry a previously unreported variant of uncertain significance (VUS) in CPA1. Determining the pathogenicity of CPA1 variants remains challenging, as disease risk is not driven by loss of enzymatic function but rather by mutation-induced protein misfolding and subsequent endoplasmic reticulum (ER) stress. Recently, two complementary approaches have been proposed to assess the pathogenic potential of CPA1 variants: (1) an in silico IA-based prediction tool, and (2) a cell-based assay using transfected HEK293T cells to measure secretion efficiency and upregulation of BiP mRNA, a marker of ER stress. Using these four cases, we aim to highlight the characteristic presentation of CPA1-related chronic pancreatitis and to evaluate the performance of these emerging tools for assessing CPA1 variant pathogenicity.

-P05-

UN UNCOMMON BILIARY OBSTRUCTION. C. Van Severen (1), R. Gillard (2) / [1] Liege University Hospital, Liege, Belgium, gastroenterology and endoscopy, [2] CHU Liege, Liège, Belgium, radiology.

This is a case report of an uncommon biliary obstruction, due to fistulization of an intraductal papillary mucinous pancreatic neoplasm (IPMN). This is a rare complication of IPMN that is not necessarily synonymous with malignancy. The mechanism of fistulization is still unclear. The most affected organs were, in decreasing order of frequency, the stomach, the duodenum, the common bile duct, and then the intestine. This case report is an opportunity to review this rare side event of the IPMN and is also the occasion to show beautiful radiological images.

DETERMINANTS OF CLINICAL SUCCESS AFTER INTERVENTIONAL THERAPY IN GENETIC CHRONIC PANCREATITIS. B. Abreu (1), I. Scheers (2), P. Deprez (3) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Brussels, Belgium, Hepato-Gastroenterology, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Brussels, Belgium, Paediatric Hepatogastroenterology, [3] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Hepatogastroenterology.

Introduction: Chronic and recurrent acute idiopathic pancreatitis remains a clinical challenge, particularly regarding the management of disease flares, interventional therapies and long-term outcomes.

Aim: This study aimed to identify potential risk and protective factors associated with clinical outcomes and to guide therapeutic management, particularly endoscopic and surgical strategies, in these patients.

Methods: We conducted a retrospective single-centre cohort study at a tertiary university hospital, including 80 consecutive patients with chronic or recurrent acute idiopathic pancreatitis carrying at least one pathogenic or likely pathogenic variant associated with hereditary or genetic pancreatitis. The main outcome was clinical remission, defined as absence of symptoms and no stent dependency at last follow-up, in patients who underwent at least one interventional treatment. Demographic, genetic, morphological and clinical variables were collected. Univariable logistic regression was used to assess predictors of clinical remission. Cox proportional hazards models were applied to evaluate time-to-event outcomes, using death, documented recurrence or ongoing stent dependency as events.

Results: Among 80 patients, 32.5% (n=26) were children (age at diagnosis <18 years) and 60% (n=48) were female. The median age at diagnosis was 27 years (IQR 13–46), and 9 years (IQR 7–13) among children. A total of 120 genetic variants were identified, including 39 CF TR, 36 PRSS1 and 28 SPINK1 mutations. A positive family history of pancreatitis was present in 28.8% (n=23). Pancreas divisum and toxic exposure were each present in 35% (n=28). Exocrine and endocrine insufficiency occurred in 33.8% (n=27) and 22.5% (n=18), respectively. One patient died from pancreatic cancer. Fifty-five patients underwent at least one interventional treatment, with a median of 2 procedures (IQR 0–5). A total of 323 interventions were performed, including 8 pancreatic resections and 7 drainage surgeries. The median disease duration at first interventional treatment was 4 years (IQR 0–9). The median total follow-up was 12.5 years (IQR 4.3–16.8), and the median followup after the last interventional treatment was 12 months (IQR 2–24). At the last clinical evaluation, 71% (n=39) of treated patients were asymptomatic and free of stenting, with a median post-interventional follow-up of 17 months (IQR 7–37) in this subgroup. In univariable logistic regression, none of the demographic, genetic or clinical variables reached statistical significance for predicting clinical remission. However, older age at diagnosis (OR 1.01; 95% CI 0.98–1.04; p=0.59) and longer disease duration at first interventional treatment (OR 1.04; 95% CI 0.96–1.13; p=0.36) trended toward higher odds of remission. Conversely, pancreas divisum (OR 0.34; 95% CI 0.10–1.12; p=0.076), toxic exposure (OR 0.39; 95% CI 0.11–1.33; p=0.13) and endocrine insufficiency (OR 0.43; 95% CI 0.12–1.54; p=0.20) trended toward lower odds of remission. In multivariable logistic regression including pancreas divisum, toxic exposure, endocrine insufficiency, disease duration at first treatment and age at diagnosis, none of the variables reached statistical significance (all p>0.10), although pancreas divisum (adjusted OR 0.44; 95% CI 0.13–1.50; p=0.19) and toxic exposure (adjusted OR 0.34; 95% CI 0.09–1.38; p=0.13) remained associated with lower odds of remission. In Cox proportional hazards analysis, pancreas divisum was associated with a higher hazard of clinical recurrence (HR 2.83; 95% CI 1.02–7.87; p=0.046), whereas no other clinical, genetic or morphological factor showed a robust association with time-to-event outcomes. Although the Cox model suggested a higher hazard of recurrence in patients with pancreas divisum (HR ≈ 2.8), the log-rank test comparing Kaplan–Meier curves did not reach statistical significance (p=0.23).

Conclusions: Despite the heterogeneity of disease expression, 71% of treated patients achieved clinical remission, indicating that most individuals derived meaningful benefit from interventional treatment management. Older age at diagnosis and longer disease duration at first interventional treatment tended to be associated with a higher likelihood of remission. Conversely, pancreas divisum, toxic exposure and endocrine insufficiency tended to be associated with a higher risk of recurrence, although these trends did not hold statistical significance.

CRONKHITE-CANADA SYNDROME: A CHALLENGING DIAGNOSIS UNDERLYING DIFFUSE GASTROINTESTINAL POLYPOSIS. J. Fallas (1), E. Besseghaier (1), N. Claeys (2), M. Gómez Galdón (3), A. Van Gossum (4) / [1] Hôpital Universitaire de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Brussels, Belgium, Centre d'Anatomie Pathologique, [2] Hôpital Universitaire de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Brussels, Belgium, Department of Colorectal Surgery, [3] Hôpital Universitaire de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Brussels, Belgium, Centre d'Anatomie Pathologique, [4] Hôpital Universitaire de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Brussels, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology.

Background & Objectives: Cronkhite-Canada syndrome (CCS) is a rare, non-hereditary gastrointestinal polyposis syndrome first described in 1955. It is characterised by diffuse gastrointestinal polyposis and protein-losing enteropathy, together with distinctive ectodermal changes affecting the skin, hair and nails: alopecia, onychodystrophy, skin hyperpigmentation and fissured tongue. Fewer than 500 cases have been reported worldwide, predominantly from Japan. CCS primarily affects adults in their sixties and has no clearly established aetiology. If left untreated, the disease tends to progress, leading to severe malnutrition, gastrointestinal bleeding and infectious complications. Historically, mortality approached 50%, but the introduction of corticosteroids, immunosuppressive therapies and nutritional support has markedly improved prognosis, with 5-year survival rates now exceeding 90%. Despite this, diagnosis remains challenging because endoscopic and histological findings are non-specific and can mimic other polyposis syndromes or hypertrophic gastropathies. We present a case of CCS that illustrates the diagnostic challenges associated with this rare condition and highlights the importance of integrating clinical, endoscopic and pathological data to reach the diagnosis.

Case presentation: A 61-year-old man with no relevant medical history developed severe gastrointestinal symptoms following a COVID-19 infection. He reported profound fatigue, loss of taste, nausea and persistent watery diarrhoea, which led to a weight loss of 35 kg over a few months, together with lower limb oedema consistent with protein loss. Upper and lower endoscopy revealed giant gastric folds, numerous gastric polyps and scattered inflammatory polyps in the duodenum and colon. Gastric biopsies demonstrated foveolar hyperplasia with marked oedema of the lamina propria, raising the possibility of Ménétrier's disease. However, the overall picture remained inconclusive, and the patient was initially managed supportively. Clinically, his condition deteriorated, with severe protein-losing enteropathy requiring parenteral nutrition that was continued at home, recurrent gastrointestinal bleeding necessitating transfusions, and progressive skin and nail changes. He developed onychodystrophy and cutaneous lesions on the chest and back, which were initially attributed to malnutrition. Persistent colonic bleeding eventually required a subtotal colectomy. Macroscopic examination of the colectomy specimen showed hundreds of polyps throughout the colon, ranging from small sessile lesions in the caecum to elongated filiform polyps in the sigmoid. Several polyps had haemorrhagic tips, corresponding to recent bleeding stigmata. Microscopically, the polyps were predominantly juvenile-type inflammatory polyps, composed of hyperplastic, sometimes cystically dilated glands within a prominently oedematous stroma rich in plasmacytes and eosinophils. No arborising smooth muscle bundles or other significant mesenchymal proliferation were identified. Importantly, the inter-polypoid mucosa was also abnormal, with glandular dilation, oedema and a dense inflammatory infiltrate. These findings, together with the clinical history and endoscopic appearance, led to the diagnosis of Cronkhite-Canada syndrome. The patient was treated with systemic corticosteroids, followed by anti-TNF- α therapy (adalimumab 40 mg every 2 weeks). He experienced marked improvement in diarrhoea, weight, and albumin levels, with resolution of his anaemia and disappearance of the skin and nail lesions. He even reported growing a fuller beard. Follow-up endoscopy showed marked regression of polyps, although microscopic abnormalities of the mucosa persisted.

Discussion: This case underlines several important points for both clinicians and pathologists. CCS is a rare condition that can also occur outside Asia and should be considered in patients with unexplained diffuse gastrointestinal polyposis and protein-losing enteropathy. Histologically, CCS polyps are non-specific, and biopsies from individual polyps alone can be misleading. Careful assessment of the inter-polypoid mucosa is therefore crucial, as glandular distortion, oedema and inflammation in otherwise unremarkable areas are key pathological clues. A multidisciplinary approach integrating clinical features, endoscopic findings and detailed pathological examination is essential for diagnosis. Ectodermal manifestations such as skin, hair and nail changes may appear late in the disease course and should not be attributed to malnutrition alone. With

timely recognition, appropriate immunosuppressive treatment and nutritional support, CCS has become a treatable condition with favourable outcomes.

-R02-

CHARACTERIZING DUODENAL INTRAEPITHELIAL LYMPHOCYTOSIS: A DESCRIPTIVE LONGITUDINAL STUDY. R. Bellamlih Mamou (1), L. Verset (2), A. Trepant (2), C. Liefferinckx (1) / [1] HUB Hôpital Erasme, Brussels, Belgium, Gastroenterology- Hepato-Pancreatology and Digestive Oncology, [2] HUB Hôpital Erasme, Brussels, Belgium, Anatomic Pathology.

Introduction: Duodenal intraepithelial lymphocytosis (IEL) corresponds to an abnormal increase in intraepithelial lymphocytes within the duodenal mucosa, generally defined as ≥ 25 lymphocytes per 100 epithelial cells. Although IEL is most encountered in celiac disease, it may also occur in a wide range of gastrointestinal and systemic conditions, and it frequently presents with nonspecific symptoms, a normal endoscopic appearance, and an absence of villous atrophy. This combination makes IEL a challenging finding for clinicians, especially given its rising incidence over the past two decades. Several hypotheses have been proposed to explain this trend, including increased access to endoscopy, systematic biopsy practices, and improved recognition of subtle histological abnormalities. Despite these factors, IEL remains a heterogeneous and often poorly understood entity. A more precise characterization of affected patients is therefore required to better guide diagnostic strategies and follow-up.

Aim: This study aimed to characterize patients with duodenal IEL by analysing their clinical, biological, endoscopic, and histological features, to identify underlying conditions associated with IEL, and to evaluate its progression over time in patients who underwent repeated endoscopies.

Methods: We performed a retrospective single-centre study including adult patients with duodenal IEL reported on biopsy between 2012 and 2024 at Erasme Hospital, Brussels. The threshold used for IEL diagnosis was ≥ 40 lymphocytes per 100 epithelial cells. Patients were excluded if they already had a known diagnosis of celiac disease prior to gastroscopy, if IEL was found exclusively in other digestive segments, or if follow-up data was not available. Clinical data such as medical history and medication use, biological tests, endoscopic findings, and histological results were extracted from electronic medical records. Clinical follow-up allowed identification of patients with or without a final diagnosis explaining the IEL. When available, follow-up endoscopies were analysed to determine IEL persistence or resolution. All data were collected after the approval of the Erasme Hospital ethics committee. Descriptive statistics summarized clinical, biological, endoscopic, and histological features. Normality was assessed using the Shapiro-Wilk test. Continuous variables were expressed as mean $\pm$ Standard deviation or median [interquartile], and categorical variables as counts and percentages. Analyses were performed using IBM SPSS Statistics.

Results: Among 592 patients identified, 311 fulfilled inclusion criteria. The cohort demonstrated a marked female predominance (75.9%, $n=236$). The mean age was 47.7 ± 16.4 years. Half of the population (49.2%) had a preexisting digestive condition, such as gastroesophageal reflux disease (34.6%), inflammatory bowel disease (22.9%), or a prior *Helicobacter pylori* infection (20.9%). Medication exposure was frequent (58.2%), with proton pump inhibitors (30%) and NSAIDs (7.4%) representing the main treatments. The main indications for gastroscopy were abdominal pain (47.9%), reflux symptoms (21.9%), and diarrhea (20.3%). The duodenal mucosa appeared normal in 85.2% of cases. Histologically, gastritis was present in 86% of gastric biopsies, whereas *H. pylori* infection accounted for 6.8%. Duodenal villous atrophy was rare (7%). A diagnostic workup was performed for most patients. Celiac serology was obtained in 76% of the cohort and was positive in 14% of those tested ($n=32$). Based on the diagnostic workup, an etiology explaining IEL was identified in 107 patients (35%). Newly diagnosed celiac disease represented the most frequent explanation ($n=48$; 45% of diagnosed cases). Other causes included inflammatory bowel disease ($n=32$), *H. pylori* infection ($n=11$), digestive infections ($n=7$), Biermer's disease ($n=4$), and drug-induced enteropathy ($n=3$). However, in most patients (65.6%), IEL remained without a definitive explanation. Follow-up gastroscopy was available for 129 patients at a median interval of 2.5 years (IQR 1.1-4.4). Duodenal biopsies demonstrated IEL persistence in 63% of cases. IEL persistence was highest when endoscopic follow-up occurred within the first year (77.8%), then decreased around 59% over the following two years. IEL resolution was most frequent in patients without identified etiology (46.4%), while patients with celiac disease had the lowest resolution rate (24.2%).

Conclusions: This study underscores the clinical challenge posed by the histological diagnosis of duodenal IEL. While celiac disease was the most frequently identified etiology, a definitive cause remained undetermined in most cases. The high prevalence of nonspecific symptoms, normal endoscopic findings, and persistent IEL over time raises questions about the role of systematic duodenal biopsies, comprehensive diagnostic workup,

and longitudinal follow-up. These findings emphasize the clinical heterogeneity of duodenal IEL and the need for further research to elucidate its underlying mechanisms and guide patients management.

-R03-

SOLID PSEUDOPAPILLARY NEOPLASM OF THE PANCREAS IN A CHILD: CONTRIBUTION OF MOLECULAR PROFILING IN A CASE REPORT. T. Scholzen (1), D. Hoton (2), P. Deprez (3), C. Dragean (4), C. Hubert (5), I. Borbath (6), G. Van Ooteghem (7), A. Caminoa (8) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Pathology, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Pathology, [3] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Gastroenterology, [4] Cliniques universitaires Saint-Luc, Brussels, Belgium, Radiology, [5] Cliniques universitaires Saint-Luc, Brussels, Belgium, Digestive Surgery, [6] Cliniques universitaires Saint-Luc, Brussels, Belgium, Oncology, [7] Cliniques universitaires Saint-Luc, Brussels, Belgium, Radiation Oncology, [8] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Pathology.

Background: Solid pseudopapillary neoplasm of the pancreas (SPNP) is a rare epithelial tumour predominantly affecting children and young women. Despite its low malignant potential, accurate diagnosis is essential to guide surgical management and avoid overtreatment. Molecular profiling, especially identification of CTNNB1 mutations, has become an important adjunct in diagnostically challenging cases.

Case Presentation: We report the case of a 9-year-old girl presenting with abdominal pain and vomiting. Abdominal imaging demonstrated a well-circumscribed pancreatic lesion with mixed solid and cystic components. The differential diagnosis included a pancreatic pseudocyst and SPNP. Diagnostic Assessment: Endoscopic ultrasound-guided fine-needle aspiration provided diagnostic material. Histology showed solid and pseudopapillary architecture composed of uniform polygonal cells with nuclear grooves, finely dispersed chromatin, and vacuolated cytoplasm. Immunohistochemistry revealed strong nuclear and cytoplasmic β -catenin positivity with loss of membranous staining, positivity for CD10, vimentin, and progesterone receptor, and focal synaptophysin expression. Cytokeratin staining was weak, and the Ki-67 index was low. Targeted sequencing identified a pathogenic CTNNB1 exon 3 mutation, confirming the diagnosis. Management: The patient underwent a distal hemipancreatectomy with complete resection and an uneventful postoperative course.

Conclusion: This case underscores the importance of considering SPNP in the differential diagnosis of Paediatric pancreatic masses. It also highlights the diagnostic utility of combining cytomorphology, immunohistochemistry, and molecular profiling—particularly CTNNB1 mutation analysis—to achieve a definitive diagnosis and guide appropriate management.

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-R04-

PANCREATIC CYSTIC LESION: IS IT ALWAYS IPMN? C. Legros (1), M. Racu (1), M. Delhay (2), M. Arvanitakis (2), D. Franchimont (2), M. Pezzullo (3), P. Loi (4), L. Verset (5) / [1] CHU Brugmann, Brussels, Belgium, Department of Pathology, [2] Hôpital Universitaire de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Brussels, Belgium, Department of Gastroenterology, [3] Hôpital Universitaire de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Brussels, Belgium, Department of Radiology, [4] Hôpital Universitaire de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Brussels, Belgium, Department of Digestive Surgery, [5] Hôpital Universitaire de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Brussels, Belgium, Department of Pathology (Centre d'Anatomie Pathologique-CAP).

Case description: We report the case of a 75-year-old man referred for evaluation of a pancreatic cystic lesion. Laboratory tests revealed isolated elevations of bilirubin and lipase, with normal CA19-9 levels. Endoscopic ultrasound identified a cystic lesion with a solid component measuring 42 mm. Cytology from fine-needle aspiration suggested an intraductal papillary mucinous neoplasm (IPMN). Thoracoabdominal CT demonstrated a mixed cystic-solid lesion in the pancreaticoduodenal groove ($72 \times 38 \times 36$ mm), which was hypermetabolic on PET scan. After multidisciplinary discussion, a pylorus-resecting pancreaticoduodenectomy was performed. Gross examination revealed a cystic lesion with a solid component filling the main pancreatic duct and containing clear, non-mucoid fluid. Microscopic analysis showed an intraductal neoplastic proliferation composed of closely packed glands. The cells exhibited marked cytonuclear atypia, and foci of microinvasion were observed. Based on these histological features, the diagnosis of intraductal tubulopapillary neoplasm (ITPN) with high-grade dysplasia and microinvasive foci was established. Seventeen lymph nodes were negative for metastasis, and no lymphovascular or perineural invasion was observed. The tumour was staged as pT1aN0. Given the absence of adverse histopathological prognostic factors, surveillance without adjuvant therapy was recommended. Seven years postoperatively, the patient remains disease-free.

Conclusion: ITPNs represent less than 1% of all exocrine pancreatic neoplasms and almost 3% of intraductal pancreatic tumours. It occurs in patients aged 25–84 years, with a slight female predominance. Unlike ductal adenocarcinomas and IPMNs, ITPNs lack common molecular alterations such as KRAS mutations. Prognosis is significantly better than ductal adenocarcinoma, with a 5-year survival rate of 71% in cases associated with invasive carcinoma.

-R05-

SOMETHING IN THE AMPULLA... IAPN: A RARE ENTITY. M. Benkaddour (1), D. Germanova (2), A. Hittet (3), J. Van Laethem (4), M. Pezzullo (5), L. Verset (1) / [1] Hôpital Universitaire de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Brussels, Belgium, Department of Pathology (centre d'anatomie pathologique-CAP), [2] Hôpital Universitaire de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Brussels, Belgium, Department of Surgery, [3] CHU Ambroise Paré MONS, Mons, Belgium, Department of Gastroenterology, [4] Hôpital Universitaire de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Brussels, Belgium, Department of Gastroenterology, [5] Hôpital Universitaire de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Brussels, Belgium, Department of Radiology.

Case description: A 79-year-old woman was referred for management of an ampullary lesion discovered following obstructive jaundice associated with pale stools, nausea, and abdominal discomfort. The patient also reported anorexia without weight loss. Thoracoabdominal CT revealed severe biliary obstruction caused by a mass measuring $25 \times 20 \times 15$ mm within the distal common bile duct, protruding into the ampulla of Vater. Precise localization was challenging based on imaging, and the pancreatic duct was not dilated. MRI confirmed marked intra- and extrahepatic biliary dilatation upstream of the lesion. A pylorus-resecting pancreaticoduodenectomy was performed. Gross examination revealed an intraductal, villous lesion centred on the ampulla and extending into the distal bile duct, measuring $31 \times 21 \times 15$ mm, without invasion of the adjacent pancreatic parenchyma. Histology demonstrated an intraductal tubulovillous growth with marked cytonuclear atypia originating from the ampullary epithelium. Based on these findings, the diagnosis of intra-ampullary tubulopapillary neoplasm (IAPN) was established. Nineteen lymph nodes were negative for metastasis. Microscopic examination also revealed millimetric invasive foci confined to the ampulla, without pancreatic parenchymal involvement; the lesion was staged as pT1aN0. Given the absence of adverse histopathological prognostic factors, imaging and laboratory surveillance was recommended.

Conclusion: IAPNs exhibit predominant growth within the ampulla and may display variable grades of dysplasia within the same lesion. Intestinal and pancreatobiliary differentiation coexist in approximately 50% of cases. Associated invasive carcinoma occurs in up to 75% of cases and may be subtle or overlooked. IAPNs without invasive carcinoma have a 5-year survival rate of 100% following complete resection.

YOUNG BELGIAN ASSOCIATION FOR THE STUDY OF THE LIVER (YBASL)

-Y01-

THE PFIB SCORES FOR PAEDIATRIC MASLD FIBROSIS ASSOCIATE WITH THE RISK OF YOUTH-ONSET TYPE 2 DIABETES IN CHILDREN WITH OBESITY. S. Lefere (1), R. Putri (2), P. Danielsson (2), T. Casswall (2), C. Marcus (2), C. Hudert (3), A. Geerts (1), R. De Bruyne (1), E. Hagman (2) / [1] Ghent University, Ghent, Belgium, Hepatology Research Unit, dpt. of Internal Medicine and Paediatrics, [2] Karolinska Institutet, Karolinska University Hospital, Sweden, Clinical Science, Intervention and Technology, [3] Charité University Hospital, Berlin, Germany, Paediatric Gastroenterology, Nephrology and Metabolic Diseases.

Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD) has become the most common liver disease worldwide in children and adolescents just as in adults. We recently developed a novel risk score, the pFIB-c, and a simplified version, the pFIB-6, for the diagnosis of significant liver fibrosis in Paediatric MASLD. Still, no Paediatric scores have been evaluated for their prognostic value in longitudinal studies.

Aim: In this study, we hypothesized that the pFIB scores are associated with the risk of type 2 diabetes (T2D) in adolescence and young adulthood, underpinning their clinical utility.

Methods: A cohort study was conducted using the Swedish Childhood Obesity Treatment Register (BORIS, 2005-2020) linked with national registers, from which T2D was ascertained. We included 4,856 children with obesity and 23,758 general population comparators. The pFIB-c (<https://www.mdcalc.com/calc/10615/Paediatric-fibrosis-score-continuous-pFIB-c>) and simplified pFIB-6 scores were calculated as published at the time of patient inclusion in the database. The incidence rate per 10,000 person-years (PY) was calculated for the general population and individuals with obesity with or without elevated pFIB scores. Time-to-event analysis yielding hazard ratio (HR) was performed using Cox regression and flexible parametric survival models.

Results: Among children with obesity, 12.4% (n = 602) had a high pFIB-6 (≥ 4). The HRs for T2D were not proportional over time, with an inflection point in late adolescence. A high pFIB-c score increased the risk for T2D at 9-19 years of age (adjusted HR 3.03, 95% CI 2.19-4.19, $p < 0.001$). The incidence rate was 1.02 (95% CI 0.61-1.72) per 10,000 PY in the general population comparators, 45.5 (95% CI 37.8-54.7) in individuals with obesity and a pFIB-6 < 4 , and 161.7 (95% CI 122.2-213.9) when the pFIB-6 ≥ 4 . Among individual score components, hypertension, ALT and HOMA-IR were associated with a greater likelihood of incident T2D, with ALT being the strongest predictor. Male sex reduced predictive performance, as girls were at higher risk of T2D. In contrast, neither score, measured at Paediatric age, predicted T2D risk at 20-25 years of age.

Conclusions: This is the first evidence of a Paediatric fibrosis score that correlates with clinically meaningful outcomes. These findings support the scores' integration into risk stratification tools for children with MASLD, while highlighting the need for longer follow-up to assess cardiovascular and liver outcomes.

-Y02-

CEUS IN MASLD: TOWARDS A NON-INVASIVE MARKER OF HISTOLOGICAL ACTIVITY. Z. Gadi (1), W. Kwanten (1), A. Driessen (2), T. Vanwolleghe (1), S. Francque (1), L. Vonghia (1) / [1] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology & Hepatology, [2] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Pathology.

Introduction: Microvascular dysfunction plays a critical yet under-investigated role in metabolic dysfunction-associated steatotic liver disease (MASLD). Time-intensity curve (TIC) analysis from contrast-enhanced ultrasound (CEUS) enables real-time quantification of hepatic micro (vascular) perfusion, offering a potential non-invasive alternative to assess MASLD severity.

Aim: This study evaluates TIC analysis from CEUS to assess MASLD, examining whether TIC parameters reflect underlying disease severity.

Methods: Patients with a clinical indication for liver biopsy because of a suspicion of MASLD were prospectively included upon IC to undergo also CEUS with subsequent TIC analyses (11 perfusion parameters) on the same day as liver biopsy. All examinations were performed in the fasting state. Associations between TIC parameters and key histological features, including steatosis, ballooning, inflammation, activity (ballooning + inflammation), fibrosis, presence of steatohepatitis (MASH) and at-risk MASH (MASH + F2-

3) were analysed. Receiver operating characteristic (ROC) analysis was additionally applied to evaluate the diagnostic performance of individual TIC parameters in predicting MASH and significant fibrosis $\geq$ F2. **Results:** Sixty-three patients with an adequate biopsy and CEUS data were included (n=56 MASLD; n=7 normal liver or minimal lesions). Among the MASLD participants, 28 had MASH. Fibrosis distribution was (F0 n=12, F1 n=13, F2 n=17, F3 n=8, F4 n=13). Risk-stratified groups hence were controls (n = 7), low-risk MASLD F0-1 (n = 14), at-risk MASH F2-3 (n = 19) and MASLD cirrhosis (F4) (n = 13). TIC parameters were negatively correlated with steatosis, including Maximum Gradient (MGrad; $\rho = -0.438$), Mean Gradient (Grad; $\rho = -0.255$), Area Under the Curve (AUC; $\rho = -0.473$), and Wash-out Area Under the Curve (WOAUC; $\rho = -0.436$). Ballooning was positively correlated with Wash-in Area Under the Curve (WIAUC; $\rho = 0.262$). Inflammation and activity showed a significant negative correlation with WOAUC (respectively $\rho = -0.334$ and $\rho = -0.302$). Fibrosis showed positive correlations with WIAUC ($\rho = 0.404$), Time-to-Peak (TTP; $\rho = 0.326$), and Time-Washout Ratio (TWR; $\rho = 0.320$), and a negative correlation with Grad ($\rho = -0.278$). In the comparison between MASH and non-MASH within MASLD, the Wash-in Area Under the Curve (WIAUC) was significantly higher in the MASH group (median 813.7 vs 692.6 AU; $p = 0.048$). Across the control, early MASLD (F0–1), at-risk MASH (F2–3), and cirrhotic MASLD (F4) groups, CEUS TIC analysis demonstrated progressive alterations in hepatic perfusion. The WIAUC increased steadily from a median of 777 AU in controls to 1,021 AU in cirrhosis ($p = 0.002$), indicating augmented enhancement with advancing fibrosis. The WOAUC, reflecting parenchymal retention, declined from 3,949 AU in controls to 2,812 AU in at-risk MASH ($p = 0.018$), consistent with compromised wash-out at intermediate disease stages. In parallel, TTP was delayed from 52.3 s in controls to 59.9 s in at-risk MASH ($p = 0.034$), while TWR increased from 0.41 to 0.49 ($p = 0.034$), reflecting prolonged enhancement kinetics. WIAUC showed fair diagnostic accuracy for MASH (AUC 0.657; 82% sensitivity, 39% specificity), while for significant fibrosis, WIAUC (AUC 0.732; 85% sensitivity, 50% specificity), TTP (AUC 0.731; 81% sensitivity, 55% specificity), and TWR (AUC 0.722; 78% sensitivity, 55% specificity) demonstrated higher discriminative performance.

Conclusions: Although many TIC-derived parameters reached significance, the overall AUC, WIAUC, WOAUC and TTP were the most consistently discriminative. All these parameters capture complementary aspects of hepatic microvascular function. Their behaviour across disease stages supports the concept of progressive vascular impairment in progressive MASH. These findings position CEUS as a promising non-invasive tool for assessing MASLD/MASH severity.

-Y03-

MUSCLE FAT CONTENT IS ASSOCIATED WITH THE PRESENCE OF STEATOTIC LIVER DISEASE, MUSCLE FUNCTION IMPAIRMENT AND INSULIN RESISTANCE. G. Henin (1), M. Nachit (2), S. André-Dumont (1), A. Goffaux (2), S. Declerck (2), A. Gouw (3), C. Sempoux (4), P. Baldin (5), P. Henry (6), G. Duchene (7), P. Trefois (7), E. Danse (7), H. Reyngoudt (8), B. Marty (8), A. Loumaye (9), P. Stärkel (1), I. Leclercq (2), N. Lanthier (1) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Brussels, Belgium, Department of Hepato-gastroenterology, [2] Université catholique de Louvain (UCLouvain), Brussels, Belgium, Brussels, Belgium, Laboratory of Gastroenterology (GAEN), Institut de Recherche Expérimentale et Clinique (IREC), [3] University Medical Centre Groningen, the Netherlands, Groningen, The Netherlands, Department of Pathology and Medical Biology, [4] Lausanne University Hospital (CHUV), University of Lausanne (UNIL), Switzerland, Lausanne, Switzerland, Institute of Pathology, [5] Cliniques universitaires Saint-Luc, Brussels, Belgium, Brussels, Belgium, Department of Pathology, [6] Institut de Pathologie et de Génétique, Gosselies, Charleroi, Belgium, Department of Pathology, [7] Cliniques universitaires Saint-Luc, Brussels, Belgium, Brussels, Belgium, Department of Imaging, [8] NMR laboratory, CEA/DRF/IBJF/MIRCen, Neuromuscular Investigation Centre, Institute of Myology, Paris, France, Paris, France, Department of NMR, [9] Cliniques universitaires Saint-Luc, Brussels, Belgium, Brussels, Belgium, Department of Endocrinology and Nutrition.

Introduction: Decreased skeletal muscle density is associated with metabolic dysfunction-associated steatohepatitis (MASH) in subjects with severe obesity. However, reliable data on muscle fat content and its related consequences are lacking in the general MASLD population and in alcohol-related liver disease (ALD).

Aim: To investigate the muscle phenotype (mass and intramuscular fat) by magnetic resonance imaging in relation to muscle function and liver disease severity, histologically assessed in a large cohort of patients with SLD.

Methods: Patients with a steatotic liver disease (SLD) were prospectively recruited from hepatology and diabetology outpatient clinics and the alcohol withdrawal unit. Patients underwent liver/skeletal muscles MRI (3.0 T, GE Healthcare®). If fibrotic SLD was suspected based on increased liver stiffness (transient elastography) (≥ 7.8 kPa), a liver biopsy was performed on that same day. Controls were recruited based on the absence of SLD on transient elastography and underwent the same MRI protocol. Liver fat content and stiffness were further measured by proton density fat fraction (PDFF) and magnetic resonance elastography (MRE). Muscle mass was estimated using the height-normalized skeletal muscle index (SMI) at the third lumbar vertebra. Intramuscular fat content from paravertebral (psoas and erector) and right leg muscles was measured using PDFF. Liver biopsies were histologically scored using the SAF score first by two local pathologists and revised by two international ones to reach consensus. Muscle function was assessed using the Liver Frailty Index (LFI) combining handgrip strength, balance and sit-to-stand tests. Insulin resistance was assessed in non-diabetic participants using the homeostasis model assessment for insulin resistance (HOMA-IR). Type 2 diabetes was defined by the daily intake of hypoglycaemic drugs. Intergroup comparisons were systematically performed by gender, analysing men and women separately to account for the physiological effects of gender on muscle phenotype.

Results: 92 participants with SLD (54 MASLD, 38 ALD) and 10 controls were included out of 118 screened participants between March 2021 and August 2024. Control and SLD groups were comparable for age (median age: 43 for controls, 57 for MASLD, 51 for ALD – $p = 0.140$). Type 2 diabetes was more prevalent in the MASLD group (33%) than in control (0%) and ALD (8%) groups ($p < 0.0001$). SLD groups did not differ in terms of liver stiffness assessed by transient elastography and magnetic resonance elastography. Steatosis was graded as 2-3 in 54% of the SLD cohort. Ballooning was graded as 0 in 50%, 1 in 23% and 2 in 27%. Fibrosis was graded as ≥ 2 in 63% of the SLD cohort. Mean muscle fat content and mass, across all examined muscles, were significantly higher in the 2 SLD groups compared to controls for both sexes (mean SMI (cm^2/m^2): 36.0 in control, 58.6 in MASLD, 47.7 in ALD – $p < 0.001$). Muscle fat content, mass and function was similar in MASLD and ALD groups in spite of clear metabolic differences. Participants with a SLD and a mean paravertebral muscles fat content above 30% consistently had an impaired muscle function (sit-to-stand, handgrip strength test and LFI) compared to participants with low ($>30\%$) muscle fat but comparable age and BMI ($p > 0.05$). The association holds true in men and in women. Insulin resistance assessed by the HOMA-IR positively correlated to mean leg fat content in MASLD ($r = 0.45$, $p = 0.017$) and in ALD ($r = 0.47$, $p = 0.005$).

Conclusions: Muscle fat content as assessed using accurate quantitative MRI technique, is increased in the presence of SLD, whether MASLD or ALD, in a large prospective cohort. This observation supports grouping MASLD and ALD into a common entity related to muscle changes, with myosteatorosis being associated with impaired muscle function and insulin resistance.

-Y04-

REAL-WORLD THERAPY RESPONSE IN PRIMARY BILIARY CHOLANGITIS: INSIGHTS FROM A BELGIAN MONOCENTRIC COHORT. J. Clerick (1), H. Van Malenstein (2), S. Van der Merwe (2), J. Verbeek (2) / [1] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Gastroenterology and hepatology, [2] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Hepatology.

Introduction: Primary biliary cholangitis (PBC) is a rare immune-mediated liver disease, characterized by progressive destruction of the intrahepatic bile ducts, leading to cholestasis, fibrosis, and, in advanced stages, cirrhosis and liver failure. Mounting evidence supports normalization of alkaline phosphatase (ALP) as the optimal treatment goal. In Belgium, bezafibrate is used off-label for patients who are non-responders or intolerant to ursodeoxycholic acid (UDCA), while newer agents such as seladelpar and elafibranor are in the process of obtaining market access approval in Europe. However, to date, no real-world observational data on therapy response in PBC patients in Belgium are available.

Aim: To evaluate biochemical treatment response and tolerability of available therapeutic agents in a representative Belgian PBC cohort, to identify predictors of inadequate biochemical response and to identify patients under active follow-up requiring additional therapy.

Methods: We performed a retrospective monocentric cohort study of 321 consecutive PBC patients initiated on UDCA between 1990 and December 2024. Biochemical response after one year UDCA treatment and biochemical response at the last available follow-up were assessed according to the POISE criteria and complete ALP normalisation. Exclusion criteria for the one-year assessment were lack of complete biochemical data ($n = 170$) and liver transplantation within the first treatment year ($n = 4$). Exclusion

criteria for the assessment at last available follow-up were death (n=118), liver transplantation (n=64) and inclusion in a PBC drug trial (n=44). Univariate Cox regression was applied to assess the relationship between variables and biochemical outcomes, multivariate Cox regression was used to adjust for possible confounding factors, using SPSS.

Results: Most patients were female (290/321, 90.3%) and AMA-positive (267/301, 88.7%). At the timepoint of start UDCA, mean age was 55.0 +/- 12.2 years, 38/291 (13%) had cirrhosis, median ALP was 325 U/L (204-502), AST 47 U/L (31-74), ALT 55 U/L (37-89), total bilirubin 0.52 mg/dl (0.41-0.82) and GGT 214 U/L (115-502). During a median follow-up of 12.2 years (6-18), 74/242 (30.6%) developed cirrhosis and 64/309 (20.7%) underwent liver transplantation. 17/321 (5.2%) patients stopped UDCA during the first year. One year after the initiation of UDCA therapy: 58/131 (44.3%) patients fulfilled the POISE criteria and 25/146 (17.1%) achieved complete ALP normalization (including patients who (temporarily) discontinued UDCA and those who received inadequate dosage). Univariate logistic regression linked higher baseline bilirubin (OR 0.041, p = 0.003), GGT (OR 0.997, p = 0.05), ALP (OR 0.992, p < 0.001), and ALT (OR 0.988, p = 0.04) to absence of complete ALP normalisation at 1 year. Multivariate logistic regression identified baseline ALP as the only independent predictor (OR 0.993, 95% CI 0.988–0.997, p = 0.002). Fibrates were initiated in 32.4% (104/321) patients, of which 24/104 (23%) actively discontinued therapy most frequently due to myalgia (8/24 (33%) and gastrointestinal complaints 4/24 (17%). Median time to discontinuation was 3 months (IQR 2-9.5). At time-point of last available follow-up, 76/93 (81.7%) fulfilled the POISE criteria and 74/133 (55.6%) achieved complete ALP normalisation. When only including patients in active follow-up 54/68 (79.4%) fulfilled the POISE criteria and 56/93 (60.2%) achieved complete ALP normalisation. After excluding patients who started fibrates less than six months before last follow-up, 49/60 (81.67%) fulfilled POISE criteria and 55/84 (65.5%) achieved complete ALP normalisation. In univariate logistic regression, higher baseline ALP (OR 0.998, p = 0.020), AMA-positivity (OR 3.045, p = 0.027) and use of fibrates at endpoint (OR 4.276, p = 0.002) were significantly associated with achieving complete ALP normalisation at the last available visit. Multivariate logistic regression confirmed baseline ALP (OR 0.998, 95% CI 0.997–1.000, p = 0.020), AMA positivity (OR 3.699, 95% CI 1.243–11.013, p = 0.019) and fibrate use at endpoint (OR 3.983, 95% CI 1.287–12.332, p = 0.017) as independent predictors for ALP normalisation. Of the 37/93 patients who did not achieve complete ALP normalisation and were under active follow-up, 18 patients never used fibrates.

Conclusions: This first Belgian real-world analysis demonstrates that fibrates are widely used in PBC patients and are independently associated with complete normalization of ALP. Nevertheless, the substantial discontinuation rate of fibrates and the proportion of patients who fail to achieve ALP normalization underscore the need for additional therapeutic options in PBC management.

-Y05-

ANTI-SONIC HEDGEHOG IMMUNOHISTOCHEMISTRY ACCURATELY DIAGNOSES BALLOONING DEGENERATION IN BOTH METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE AND ALCOHOL-RELATED LIVER DISEASE. G. Henin (1), S. Declerck (2), A. Goffaux (2), P. Baldin (3), P. Henry (4), C. Bouzin (5), I. Leclercq (2), P. Stärkel (1), A. Gouw (6), C. Sempoux (7), N. Lanthier (1) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Brussels, Belgium, Department of Hepato-gastroenterology, [2] Université catholique de Louvain (UCLouvain), Brussels, Belgium, Brussels, Belgium, Laboratory of Gastroenterology (GAEN), Institut de Recherche Expérimentale et Clinique (IREC), [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Brussels, Belgium, Department of Pathology, [4] Institut de Pathologie et de Génétique, Gosselies, Charleroi, Belgium, Department of Pathology, [5] IREC Imaging Platform (2IP), Institut de Recherche Expérimentale et Clinique (IREC), UCLouvain, Brussels, Belgium, Brussels, Belgium, Imaging platform, [6] University Medical Centre Groningen, the Netherlands, Groningen, The Netherlands, Department of Pathology and Medical Biology, [7] Lausanne University Hospital (CHUV), University of Lausanne (UNIL), Switzerland, Lausanne, Switzerland, Department of Pathology.

Introduction: Ballooning degeneration is a key histological marker of steatotic liver disease (SLD) severity, but it remains difficult to identify reliably and shows poor inter-observer agreement. Sonic hedgehog (SHH) pathway is involved in ballooning pathogenesis in metabolic dysfunction-associated steatotic liver disease. But data on the expression of SHH ligand in other SLD subtype including alcohol-related liver disease (ALD), and the diagnostic accuracy of anti-SHH immunohistochemistry (IHC) in real-life practice are lacking.

Aim: To assess the diagnostic accuracy of anti-SHH IHC for the diagnosis of ballooning degeneration in SLD.

Methods: Participants were prospectively recruited from hepatology outpatient clinics and the alcohol withdrawal unit. Prospectively recruited participants with a diagnosis of SLD (MASLD or ALD) on imaging and increased liver stiffness (≥ 7.8 kPa, M probe, Fibroscan®) underwent liver biopsy. Four blinded pathologists scored haematoxylin-eosin stained slides for steatosis and activity including ballooning. Anti-SHH IHC was performed on the same liver samples and quantified manually (positive cells per field at 40-fold magnification) by two untrained observers blinded to the pathology score. SHH positive cells are expressed as mean positive cells between the two observers and divided by total number of examined fields.

Results: Eighty-eight participants with SLD (52 with MASLD, 36 with ALD) were prospectively recruited and underwent liver biopsy. Median self-reported alcohol consumption was 80 units per week in the ALD group. Mean BMI was significantly higher in the MASLD group (34.7 kg/m^2) compared to the ALD group (27.3 kg/m^2 ; $p < 0.0001$). 38% of cases were classified by pathologists as fibrosis grade 0-1 (F0-1), 30% as F2, 26% as F3 and 6% as F4 in the pooled SLD group. 46% of MASLD cases were classified as ballooning grade 0 (B0), 27% as B1 and 27% as B2 while 61% of ALD were classified as B0, 14% as B1 and 25% as B2. The count of SHH positive cells strongly correlated between untrained observers ($r = 0.89$, $p < 0.0001$) across the whole SLD cohort. SHH positive density positively correlated with ballooning grades in MASLD ($r = 0.71$, $p < 0.0001$), ALD ($r = 0.75$, $p < 0.0001$) and pooled SLD ($r = 0.69$, $p < 0.0001$). In particular, the median SHH density was 0.03 for B0, 0.16 for B1 and 0.96 for B2 in the pooled SLD group ($p < 0.0001$). SHH density showed a very high diagnostic accuracy for the diagnosis of ballooning in MASLD (AUC = 0.83, $p < 0.0001$), ALD (AUC = 0.94, $p < 0.0001$) and pooled SLD (AUC = 0.86, $p < 0.0001$).

Conclusions: Anti-SHH IHC is a highly accurate tool for the diagnosis of ballooning by untrained observers in MASLD and ALD highlighting its potential utility in clinical practice and research in the topic of SLD.

-Y06-

DEVELOPMENT OF A CARE PATHWAY FOR PATIENTS WITH LIVER CIRRHOSIS. L. Seynhaeve (1), C. De Vloo (2), S. De Meulder (2), J. Dewyspelaere (2), L. Harlet (2), K. Ferdinande (3), E. Puttevils (4), J. Decaestecker (2) / [1] AZ Delta, Roeselare, Belgium, Department of Hepatology, Rumbeke, Belgium, [2] AZ Delta, Belgium, Department of Gastroenterology and Hepatology, Rumbeke, Belgium, [3] Ghent University, Ghent, Belgium, Department of Gastroenterology and Hepatology, [4] AZ Delta, Belgium, Management Department, Rumbeke, Belgium.

Introduction: Patients with cirrhosis have complex and fluctuating care needs that require coordination between hospital-based specialists and primary care providers. While decompensated cirrhosis requires frequent and intensive in-hospital multidisciplinary management, patients with compensated cirrhosis are generally managed in primary care, with considerably less intensive monitoring. For these patients, hepatology follow-up is typically scheduled every six months to allow for comprehensive assessment, including HCC surveillance with ultrasound and AFP, screening for covert hepatic encephalopathy, and evaluation of disease progression and associated comorbidities. The complexity and high prevalence of liver cirrhosis, combined with the need for multidisciplinary collaboration across hospital and primary care settings, highlight the importance of a structured and coordinated approach. (1,2)

Aim: To address the variability in clinical care, promote continuity of care, and improving patient outcomes, the aim of this project was to develop a structured care pathway for patients with cirrhosis.

Methods: A care pathway for patients with liver cirrhosis was developed at AZ Delta Hospital (Rumbeke, Belgium), following a simplified version of the seven-phase model of the Network of Clinical Paths, KU Leuven (3,4). A phase model guided the pathway's development, including screening, project management, diagnostic and objectification, development, and finally implementation, evaluation, and continuous follow-up.

Results: PHASE 1: Screening Key stakeholders were identified, including patients, family members, hepatologists, the nurse specialist, and GPs. Quality indicators (process, structure, and outcome) were defined, and a hepatology dashboard was developed to monitor admissions, readmissions, and frailty assessments. PHASE 2: Project Management The scope of the care pathway was defined, covering the entire trajectory from diagnosis to transplantation or death, for both compensated and decompensated cirrhosis. Exclusion criteria are patients in a palliative phase and those with HCC receiving non-curative treatment. A core working group was established, consisting of a hepatologist, the hepatology nurse specialist, and a care manager. PHASE 3: Diagnostic & Objectification The current care process was analysed through record

reviews and discussions with clinical teams. Key bottlenecks were identified, such as poor follow-up and limited communication between care levels. As no suitable digital system was available, a communication booklet was introduced for use between hospital and GPs. Patient interviews highlighted the need for clear information and support, shaping a patient-centred pathway design. Recent EASL (5-7) and Baveno (8) guidelines were reviewed. Most of these sources focus primarily on medical management. Limited evidence exists on hospital-based care pathways for cirrhosis; however, studies have reported positive effects of coordinated interventions on survival and readmission rates as well as on the growing and important role of specialized nurses in the care of this patient population. (9-11) PHASE 4: Development The pathway was structured around key care moments such as diagnosis with its initial assessment, hospitalization, and follow-up (figure 1). In collaboration with a digital health company, a patient app was developed to support self-management, allowing daily monitoring (weight, stool frequency), complete quality-of-life questionnaires and providing short educational videos on cirrhosis and nutrition. PHASES 5-7: Implementation, Evaluation & Continuous Follow-up Implementation is ongoing in the hepatology department, focusing on inpatients and post-discharge care. The communication booklet and patient app were introduced in 2025. Evaluation will assess adherence, patient satisfaction, and quality indicators, ensuring continuous improvement and sustainability of high-quality, evidence-based, patient-centred care. **Conclusions:** By developing this care pathway, we aim to strengthen the coordination and overall quality of care for patients with cirrhosis. The integration of a patient-centred digital app, empowers patients to actively engage in managing their disease. Ultimately, the pathway bridges the gap between hospital and primary care settings and provides a sustainable framework for continuous quality improvement.

-Y07-

RELINK HEPATITIS C: RELINKING DIAGNOSED BUT UNTREATED (DBU) HEPATITIS C PATIENTS BACK INTO CARE. K. Demeyer (1), S. Vanden Dries (1), S. Francois (1), H. Degroote (1) / [1] UZ Brussel, Brussels, Belgium, Gastroenterology and hepatology department.

Introduction: Hepatitis C virus (HCV) infection remains a leading cause of chronic liver disease, cirrhosis, and hepatocellular carcinoma globally, affecting approximately 58 million individuals worldwide. The introduction of direct-acting antivirals (DAAs) has revolutionised HCV treatment, achieving sustained virologic response (SVR) rates exceeding 95%. These advances have positioned HCV eradication as a feasible public health objective, with the World Health Organization (WHO) establishing ambitious targets for 2030: diagnosing 90% of infected individuals and treating 80% of eligible patients with chronic HCV. While Belgium has made substantial progress toward these elimination goals, current trajectories suggest our country will fall short of WHO goals by 2030. A significant challenge lies in the substantial proportion of patients lost to follow-up (LTFU) after initial diagnosis, which undermines national elimination strategies. However, LTFU patients represent a critical opportunity for targeted micro-elimination initiatives through structured patient retrieval programs.

Aim: This study aimed to evaluate the proportion of LTFU patients among anti-HCV positive patients in the UZ Brussel database between 2012-2022, recall eligible patients, and assess barriers to follow-up.

Methods: A combined retrospective-prospective study was conducted at UZ Brussel. The study population comprised adult patients (≥ 18 years) testing positive for anti-HCV antibodies between 2012 and 2022. Exclusion criteria included patients with documented virologic cure or negative HCV RNA testing. LTFU patients were identified through comprehensive medical record review. Eligible patients were systematically contacted via telephone and email to facilitate re-engagement in care and offer DAA treatment. Primary outcomes included virologic response, fibrosis staging, and identification of barriers preventing continuous follow-up.

Results: Among 744 patients with positive anti-HCV serology, 122 (16.4%) were classified as LTFU. Of these, 47 (38.5%) were eligible for retrieval and 22 (46.8%) were successfully contacted. Nineteen patients underwent HCV RNA testing, of whom 15 (78.9%) were viraemic and initiated DAA therapy. The majority of patients (66.7%) presented with minimal fibrosis (F0-F1). Common barriers to follow-up included outdated contact information, unawareness of positive HCV status, prior ineligibility for treatment, and lack of referral to the gastroenterology (GE) department. Notably, 42.6% of eligible patients had never undergone confirmatory RNA testing in the past.

Conclusions: Retrieval of LTFU patients with chronic HCV is both feasible and highly relevant to HCV elimination strategies. This study provides valuable insights into strategic approaches for re-engaging LTFU patients as a pathway toward successful HCV eradication. Despite logistical and systemic barriers, targeted retrieval strategies can achieve high treatment uptake and substantially reduce disease burden. Policy

interventions including reflex RNA testing, establishment of a centralised HCV registry, and enhanced data sharing mechanisms are essential to strengthen linkage to care and support Belgium's progress toward WHO elimination goals by 2030.

-Y08-

DIAGNOSTIC ACCURACY OF NON-INVASIVE MODELS FOR DETECTING PORTAL HYPERTENSION IN METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE. Z. Gadi (1), R. Hajj (2), E. Ehomah (3), L. Flores Ribeiro (4), L. Schoenmakers (1), L. Vonghia (1), W. Kwanten (1), T. Vanwolleghem (1), S. Francque (1) / [1] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology & Hepatology, [2] American University of Beirut (AUB) Faculty of Medicine, Beirut, Lebanon, Beirut, Lebanon, Faculty of Medicine, [3] University of Ghana Medical school, Accra, Ghana., Ghana, Andorra, Medical school, [4] Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal, Lisbon, Portugal, Faculdade de Medicina.

Introduction: Portal hypertension (PH) is a major determinant of clinical outcomes in chronic liver disease, yet its gold-standard assessment through hepatic venous pressure gradient (HVPG) measurement remains invasive and available only in specialist centres. Non-invasive tests (NITs) integrating elastography and biochemical markers may offer a practical alternative, but their performance a real-world population with metabolic dysfunction-associated steatotic liver disease (MASLD) is insufficiently characterised.

Aim: To compare the diagnostic accuracy of established and emerging NITs against HVPG for detecting portal hypertension (PH) and clinically significant portal hypertension (CSPH) in a MASLD cohort.

Methods: From a cohort of 446, a total of 232 consecutive MASLD cases undergoing transjugular HVPG measurement and liver biopsy between January 2018 and December 2024 were analysed. The following NITs were evaluated: NICER; MODEL-3P (PROB10, PRED); MODEL-5P (PROB10, PRED); ANTICIPATE (RISK CSPH); ANTICIPATE-NASH (RISK CSPH); LSPS; Lok; FIB-4+; FIB-4; MAF-5; APRI; Forns Index; AGILE3+; and AGILE4. Performance was assessed for PH (HVPG ≥ 5 mmHg) and CSPH (HVPG ≥ 10 mmHg) using area under the receiver operating characteristic curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

Results: Among the 232 patients, 81 (66%) had PH (mean HVPG 12.8 ± 5.9 mmHg, range 5-26), 47 (38%) had CSPH (mean HVPG 17.0 ± 3.8 mmHg, range 10-26), and 42 (18%) demonstrated normal portal pressure (mean HVPG 3.24 ± 0.88 mmHg). Across the cohort, NITs showed consistently high diagnostic performance. For PH detection, several models achieved AUC values ≥ 0.90 . NICER had the highest accuracy (AUC 0.929; sensitivity 0.86; specificity 1.00; PPV 1.00; NPV 0.69), while ANTICIPATE (AUC 0.912; sensitivity 0.93; specificity 0.70) and ANTICIPATE-NASH (AUC 0.909; sensitivity 0.93; specificity 0.70) similarly demonstrated robust accuracy. FIB-4+ (AUC 0.907) and the Lok Index (AUC 0.923) also provided reliable discrimination. For CSPH, performance remained excellent, with AUC values ≥ 0.90 in several models. AGILE4 showed the highest accuracy (AUC 0.936; sensitivity 0.93; specificity 0.70), followed by AGILE3+ (AUC 0.918) and NICER (AUC 0.904; sensitivity 0.95; NPV 0.95). ANTICIPATE-NASH (AUC 0.914) and ANTICIPATE (AUC 0.917) also performed well, both offering sensitivities and NPVs above 0.88, supporting their utility for safe exclusion of CSPH.

Conclusions: In MASLD, non-invasive models that incorporate elastography and portal hypertension-specific models provide high diagnostic accuracy for both PH and CSPH, consistently outperforming fibrosis-related scores. Elastography-based NITs, particularly NICER, AGILE4, and ANTICIPATE models, offer strong sensitivity and excellent NPVs, supporting their use as reliable alternatives to invasive HVPG especially for ruling out clinically significant portal hypertension in MASLD.

-Y09-

CHARACTERIZATION OF THREE METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE CLUSTERS IN A REAL-LIFE COHORT AND THEIR ASSOCIATION WITH LIVER STIFFNESS EVOLUTION. S. André-Dumont (1), G. Verwilghen (1), G. Henin (1), R. Gason (2), J. Scholtens (2), N. Lanthier (1) / [1] UCLouvain, Cliniques universitaires Saint-Luc, Belgium, Service d'Hépatogastroentérologie, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'Hépatogastroentérologie.

Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a large spectrum of conditions with possible hepatic and extra-hepatic outcomes. A recent groundbreaking analysis revealed

that patients can be classified into three main clusters based on routine clinical data: controls (CTRL), liver-specific steatotic liver disease (LS-SLD) and cardiometabolic (CM-SLD) (Raverdy et al. Nat Med. 2024).

Aim: To determine the prevalence and clinical profile of MASLD clusters in a single-centre external cohort and assess the association with baseline and follow-up liver stiffness measurement (LSM).

Methods: Patients with MASLD diagnosed by transient elastography were prospectively included and followed. LSM and controlled attenuation parameter (CAP) were recorded at baseline and follow-up. MASLD clusters (CTRL, LS-SLD and CM-SLD) were determined using the clustering tool based on age, body mass index (BMI), glycated haemoglobin (HbA1c; calculated from the latest available blood glucose when HbA1c was missing), alanine aminotransferase (ALT), triglycerides (TG) and low-density lipoprotein-cholesterol (LDL-C). Relative changes in LSM (%) at one- and three-year of standard follow-up (1Y-FU, 3Y-FU) compared to baseline were used to assess longitudinal evolution. Results are presented as median.

Results: 438 patients diagnosed with MASLD were recruited. Their median age was 54 years, 51 % were male, with a median BMI of 32.0 kg/m², HbA1c of 5.6 %, ALT of 45 IU/L, LDL-c of 105 mg/dL and TG of 150 mg/dL. Median LSM was 7.9 kPa with 55 % having $\geq$ F2 stage and median CAP was 325 dB/m with 75 % at S3 stage. MASLD clustering identified 45 % CTRL, 16 % LS-SLD and 8 % CM-SLD. 31 % were non-classified due to missing data. Compared to CTRL and LS-SLD groups, CM-SLD were older (55 vs. 45 vs. 61 years; $p < 0.001$) with similar gender distribution across clusters. Compared with CTRL and LS-SLD, CM-SLD had substantially higher HbA1c (5.5 vs. 5.5 vs. 8.0 %; $p < 0.001$), blood glucose (100 vs. 103 vs. 155 mg/dL; $p < 0.001$) and greater prevalence of type 2 diabetes (32 vs. 31 vs. 92 %; $p < 0.001$). They also showed higher TG (135 vs. 161 vs. 188 mg/dL; $p < 0.001$), prevalence of dyslipidemia (36 vs. 24 vs. 78 %; $p < 0.05$) and hypertension (49 vs. 31 vs. 89 %; $p < 0.01$). The incidence of past cardiovascular events is also doubled, although this difference is not statistically significant (13 vs. 11 vs. 24 %; $p > 0.05$). CM-SLD also had higher baseline LSM (7.2 vs. 7.9 vs. 11.9 vs.; $p < 0.001$) and higher prevalence of $\geq$ F2 (48 vs. 53 vs. 87 %; $p < 0.001$). CTRL had lower CAP compared to CM-SLD (317 vs. 330 vs. 344; $p < 0.001$). Compared with CTRL, LS-SLD and CM-SLD presented higher aspartate aminotransferase (26 vs. 48 vs. 41 IU/L, $p < 0.001$), γ -glutamyl transferase (42 vs. 77 vs. 62 IU/L; $p < 0.001$) and ALT levels (34 vs. 87 vs. 53 IU/L; $p < 0.001$). In addition, ALT was higher in LS-SLD than CM-SLD. Follow-up attendance was 62 % at 1Y-FU and 41 % at 3Y-FU. CTRL were more likely to return at 1Y-FU than LS-SLD (69 vs. 56 vs. 65 %; $p < 0.05$). At 3Y-FU, despite similar weight loss across clusters (-2.2 vs. -2.9 vs. -4.0 %, NS), CM-SLD showed greater improvement in LSM than CTRL (-1.4 vs. -12.8 vs. -21.1 %; $p < 0.05$). LS-SLD showed a numerically great improvement in LSM but without reaching statistical significance. Consistently, the proportion of patients improving their LSM ≥ 20 % was higher in LS-SLD and CM-SLD compared with CTRL (23 vs. 46 vs. 53 %; $p < 0.05$).

Conclusions: MASLD clustering is applicable in a real-life single-centre cohort and discriminates patients into subgroups. Clinical data non-included in the score and transient elastography confirm that this classification is discriminatory. CTRL patients have lower CAP and CM-SLD patients have higher LSM and hypertension. Longitudinal data show that standard care can reduce the severity of the liver disease in both LS-SLD and CM-SLD clusters. This suggests that this tool could be used in routine practice to better guide patient care.

-Y10-

THE IMPACT OF PHARMACEUTICAL INTERVENTIONS ON THE MANAGEMENT OF HOSPITALIZED PATIENTS WITH CIRRHOSIS: WHAT ROLE DOES THE CLINICAL PHARMACIST PLAY? A. Casterman (1), V. VandenDriessche (2), A. Vandenbergh (1), B. Dubois (1), O. Dalleur (3), P. Yengue (4), H. Vandenbulcke (4) / [1] Centre Hospitalier Wallonie Picarde (CHWAPI), Tournai, Belgium, Pharmacy, [2] Hôpitaux Universitaires de Bruxelles (HUB), Université Libre de Bruxelles (ULB), Belgium, Gastroenterology, [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Brussels, Belgium, Pharmacy, [4] Centre Hospitalier Wallonie Picarde (CHWAPI), Tournai, Belgium, Gastroenterology.

Introduction: Cirrhotic patients, characterized by a hepatic impairment, are at higher risk of drug related adverse events compared to the general population. Henceforth, when it comes to pharmacological treatments, choosing the right molecule and/or adapting the dose to the hepatic function should be at the forefront. Clinical pharmacists have demonstrated significant contributions across various medical fields, enhancing patient care through tailored interventions. Pharmaceutical interventions (PIs) are pharmacist-proposed actions, developed in collaboration with treating physicians, to optimise treatments

for safety and effectiveness. However, the integration of clinical pharmacists into gastroenterology care, particularly for patients with hepatic insufficiency, is limited. The adaptation of drug dosages in the context of hepatic impairment is a complex issue that lacks comprehensive discussion in current literature and practice, pointing to a significant opportunity for advancing patient care through targeted pharmaceutical strategies.

Aim: This study aims to assess the impact of pharmaceutical interventions (PIs) by a clinical pharmacist in the management of hospitalized cirrhotic patients. This study has two secondary objectives. Firstly, the adherence to the Baveno VII criteria - addressing the management of portal hypertension - regarding the prescription of beta-blockers, will be investigated. Secondly, the medication reconciliation process upon hospital discharge will be verified through contact with community pharmacies.

Methods: This prospective, monocentric, interventional study was conducted over a 12-week period at a secondary care hospital in Belgium. Thirty patients were included, of which 73.3% had alcohol-related cirrhosis. A clinical pharmacist was physically present in the gastroenterology ward and provided daily treatment recommendations or PIs, taking into account the degree of hepatic impairment. These PIs were subsequently reassessed by an expert committee composed of a hepatologist and a clinical pharmacist, using an evaluation grid adapted from the Society of Hospital Pharmacists of Australia (SHPA).

Results: A total of 143 PIs were proposed, of which 84% were fully accepted by the treating physicians, demonstrating their clinical relevance. The most frequent PIs included initiation of treatment (35.7%), dose adjustments (21.7%), and treatment discontinuation (11.9%). Of the 58 cirrhosis-specific PIs, the expert panel classified 81.0% as high-risk according to the hepatologist, and 44.8% as high-risk according to the clinical pharmacist. Betablockers (36.2%), psycholeptics (13.8%), and hypolipidemic agents (12.0%) were the most commonly involved drug classes. The level of agreement between the two experts, measured using Cohen's kappa coefficient, ranged from 0.190 to 0.450, indicating slight to moderate concordance. This variability in risk perception underscores the complexity of pharmaceutical interventions in cirrhotic patient care and the subjective nature of evaluating such interventions. Regarding Baveno VII criteria, 20% of eligible patients (n = 25) did not receive non-cardioselective beta-blockers (NCBBs) upon discharge, despite adequate blood pressure parameters. However, 5 patients were discharged from the hospital with a NCBB, which was not prescribed at admission, including 3 (12%) thanks to the pharmacist's intervention. This discrepancy suggests insufficient awareness or challenges in implementing these criteria, particularly among physicians in training. Furthermore, the study identified a critical communication gap. Out of 11 community pharmacies, three were not informed of treatment modifications at discharge, potentially compromising continuity of care. This highlights the need for improved communication channels between hospital and community pharmacies.

Conclusions: This study suggests a valuable contribution of a clinical pharmacist to the management of hospitalized cirrhosis patients. With an 84% acceptance rate by treating physicians and a high proportion of high-risk interventions, PIs demonstrate clinical relevance and potential to prevent serious drug-related events in cirrhotic patients. The study advocates for greater integration of pharmacist-led interventions in gastroenterology and enhanced collaboration among healthcare professionals to ensure comprehensive patient care and adherence to established guidelines.