

ABSTRACTS

XXXIth Belgian Week of Gastroenterology 2019

ABSTRACTS

- A01 — A37 Belgian Association for the Study of the Liver (BASL)
Belgian Liver Intestine Committee (BLIC)
- B01 — B21 Belgian Network on Gastrointestinal Regulatory Mechanisms (GIREM)[®]
- C01 — C12 Case Reports
- G01 — G17 Belgian Society for Gastrointestinal Endoscopy (BSGIE)
- I01 — I30 Belgian Inflammatory Bowel Disease Research and Development Group (BIRD)
- K01 — K09 Belgian Society for Pediatric Gastroenterology, Hepatology and Nutrition (BeSPGHAN)
- M01 — M02 Belgian Working Group on Proctology
- O01 — O19 Belgian Group for Digestive Oncology (BGDO)
- P01 — P05 Belgian Pancreatic Club (BPC)
- R01 — R09 Belgian Working Group on Digestive Pathology

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

- A01 -

THE SPDGFR-BETA CONTAINING PRTA-SCORE IS A NOVEL DIAGNOSTIC ALGORITHM FOR SIGNIFICANT LIVER FIBROSIS IN PATIENTS WITH VIRAL, ALCOHOLIC, AND METABOLIC LIVER DISEASE. J. Lambrecht (1), S. Verhulst (1), I. Mannaerts (1), J. Sowa (2), J. Best (2), A. Canbay (2), H. Reynaert (1), L. Van Grunsven (1) / [1] Vrije Universiteit Brussel (VUB), Jette, Belgium, Department of Basic Biomedical Sciences, Liver Cell Biology Laboratory, [2] University Hospital Magdeburg, Germany, Department of Gastroenterology, Hepatology and Infectious Diseases.

Introduction : Diagnosis of liver fibrosis onset and regression remains a controversial subject in the current clinical setting, as the gold standard remains the invasive liver biopsy. Multiple novel non-invasive markers have been proposed but lack sufficient sensitivity and specificity for diagnosis of early stage liver fibrosis. Platelet Derived Growth Factor Receptor beta (PDGFR β) has been associated to hepatic stellate cell activation and has been the target of multiple therapeutic studies. However, little is known concerning its use as a diagnostic agent.

Aim : In this study, we analysed the diagnostic potential of PDGFR β for liver fibrosis in a heterogenous patient population.

Methods : The study cohort consisted of 148 patients with liver fibrosis/cirrhosis due to various causes of liver injury (metabolic, alcoholic, viral), and 14 healthy individuals as control population. A validation cohort of 57 patients with metabolic liver disease, who underwent liver biopsy to stage fibrosis, were gathered. Circulating soluble PDGFR β (sPDGFR β) levels were determined using a commercial ELISA kit. The diagnostic performance of sPDGFR β as individual parameter, or in combination with other biochemical and metabolic factors was evaluated, and values were compared to those obtained by the clinical diagnostic algorithms Fib-4, APRI, and AST/ALT ratio.

Results : In the total patient population, sPDGFR β levels were progressively augmented with increasing fibrosis stage. Circulating sPDGFR β levels were elevated ($p < 0.0001$) in patients with significant fibrosis ($F \geq 2$), compared to no or mild fibrosis ($F0/1$), with a discriminative capacity, as quantified by AUC, of 0.7303, which was shown to be higher for this cohort than the AUCs of Fib-4, APRI, and AST/ALT ratio. The accuracy of sPDGFR β could be increased by combining it with albumin levels and platelet counts into a novel diagnostic algorithm, which we termed the PRTA-score. Using a cut-off value of 7.804; a sensitivity of 77.11% and a specificity of 73.17% could be obtained for the diagnosis of significant fibrosis ($F \geq 2$). AUC values for the prediction of advanced liver fibrosis ($F \geq 3$) and cirrhosis ($F = 4$) were respectively 0.7470 and 0.7995; values which are slightly better, or comparable to Fib-4, APRI, and AST/ALT ratio. The diagnostic value of sPDGFR β levels and the PRTA score were confirmed in an independent patient cohort, suffering from metabolic liver disease, which were staged for fibrosis by liver biopsy.

Conclusions : We put forth the PRTA score as an easy applicable, low cost and accurate scoring for significant liver fibrosis. With validation in larger patient cohorts, this serological test could become an important tool in future non-invasive clinical assessment of liver fibrosis.

- A02 -

A LONGITUDINAL STUDY OF SKELETAL MUSCLE ALTERATIONS IN NAFLD. M. Nachit (1), M. De Rudder (1), Y. Horsmans (2), G. Vande Velde (3), I. Leclercq (1) / [1] Institut de Recherche Expérimentale et Clinique (IREC), Catholic University of Louvain (UCL), Belgium, Pôle d'Hépto-gastro-entérologie (GAEN), [2] Saint-Luc University Hospital, Brussel, Belgium, Service D'Hépto-Gastro Entérologie, [3] KU Leuven, Belgium, Department of Imaging and Pathology.

Introduction : Non-alcoholic fatty liver disease (NAFLD) represents a spectrum of disease ranging from benign steatosis to non-alcoholic steatohepatitis (NASH). Unlike simple steatosis, hepatocellular injury and inflammation in NASH likely promote fibrosis and evolution to end-stage liver disease. Skeletal muscle, the largest body compartment, has mechanical, metabolic and endocrine functions. Cross-sectional studies clearly linked low muscularity (sarcopenia) to risk of having NAFLD and to severity of NASH-associated fibrosis. Yet it is still not clear whether low muscle mass is a cause, an aggravating factor, a consequence of the ongoing disease or an epiphenomenon reflecting general alteration in NAFLD.

Aim : To longitudinally evaluate changes in muscle compartment according to liver pathology in NAFLD mouse models.

Methods : For over 26 weeks, we followed WT mice fed a standard chow as controls (Ctl), WT mice fed a high fat (HF) diet (60% fat) as a model of simple steatosis (WT HF) and *foz/foz* mice fed a HF diet as a model of progressive NASH (FOZ HF). We performed monthly micro-computed tomography to monitor changes in body composition, skeletal muscle and liver fatty infiltration (expressed as muscle or liver density to spleen density ratio). We used grip strength test to follow muscle functionality and analyzed liver histology at monthly intervals.

Results : Ctl had normal liver histology, WT HF developed obesity and isolated mild steatosis, FOZ HF exhibited obesity and fatty changes at 4 and 8 weeks and histologically proven NASH (NAS>5) from 12 weeks up to NAS=8 from week 20 on. Muscle strength was similar in all groups up to week 8, but significantly decreased starting from week 12 in mice with NASH (Ctl : 244±4g; WT HF : 251.9±6g vs FOZ HF : 228.6±4g) and further worsened with time (188.67±8g at 26W in FOZ HF) while it remained stable in other groups. Muscle density was significantly lower in FOZ HF as early as 4 week (0.79±0.02) than in Ctl (0.91±0.02); reached a minimum at 12W (0.37±0.05 in FOZ HF vs 0.85±0.02 and 0.75±0.02 in Ctl and WT HF), then plateaued. Over the study period, liver density remained stable in Ctl [0.74-0.92], gently decreased in WT HF from 0.92 to 0.40±0.11 at 26W and followed a V-shaped curve in FOZ HF (0.89±0.02 at 0W; -0.07±0.05 at 26W), with minimal density at 12 week (-1.37±0.14). Liver density correlated with biochemical quantification of liver lipid content ($r^2=0.92$, $p<0.0001$).

Conclusions : Our results show remarkable skeletal muscle alterations concurrently to NASH onset and independently of body weight change, inviting to explore the pathophysiological role of muscle-liver axis in NASH pathogenesis and progression.

- A03 -

NON-ALCOHOLIC STEATOHEPATITIS SIGNIFICANTLY DECREASES MICROSOMAL LIVER FUNCTION IN THE ABSENCE OF FIBROSIS ALLOWING THE USE OF THE 13C-AMINOPYRINE BREATH TEST FOR ITS NON-INVASIVE DETECTION. E. Van Mieghem (1), L. Depauw (1), W. Verlinden (2), J. Weyler (3), P. Michielsen (3), L. Vonghia (3), T. Vanwollegem (3), E. Dirinck (4), L. Van Gaal (4), S. Francque (3) / [1] University of Antwerp, Antwerp, Belgium, Laboratory of experimental medicine and pediatrics, [2] AZ Nikolaas, Sint-Niklaas, Belgium, Gastroenterology and hepatology, [3] Antwerp University Hospital, Edegem, Belgium, Gastroenterology and Hepatology, [4] Antwerp University Hospital, Edegem, Belgium, Endocrinology, Diabetology and Metabolism.

Introduction : Non-alcoholic fatty liver disease (NAFLD) has become the most frequent cause of chronic liver disease in Western countries, with an increasing prevalence. The presence of non-alcoholic steatohepatitis (NASH) can lead to a more aggressive clinical course with fibrosis progression and hepatocellular carcinoma, which necessitates early NASH detection. Currently, the diagnosis of NASH is based on histology, though with the high prevalence of NAFLD, a non-invasive method is needed. The 13C-aminopyrine breath test (ABT) evaluates the function of the cytochrome P450 enzymes of the liver (microsomal liver function) and could be a potential candidate.

Aim : We aimed to firstly, evaluate a potential change in liver microsomal function in NASH patients; and secondly, to evaluate the diagnostic power of ABT to detect both NASH and fibrotic NASH (NASH-F2-4).

Methods : A retrospective analysis was performed on consecutive patients suspected of NAFLD who underwent a liver biopsy and ABT between 2002 and 2018 at the Antwerp University Hospital. Subgroups were created for patients without NASH (noNASH), patients with NASH but without significant fibrosis (NASH-noF) and patients with NASH and significant fibrosis (NASH-F).

Results : 421 patients were included (37.8 % noNASH and 62.2% NASH with 41.8% NASH-noF and 20.4% NASH-F). A significant difference in ABT was found between noNASH and NASH-noF ($p=0.011$) and between NASH-noF and NASH-F ($p<0.001$) with a cumulative excretion of 14.5 ± 6.65 , 12.8 ± 5.35 and 9.8 ± 5.16 %dose, respectively. The cumulative excretion (cABT) proved a better predictor of NASH and fibrosis than peak excretion. The predictive power of cABT as a single test was low for NASH and NASH-F with AUROCs of 0.620 and 0.650, respectively. A predictive model was created adding ALT, C-peptide and age to cABT, which increased the AUROC to 0.775 to detect NASH. A model adding AST to cABT increased the AUROC to 0.796 to detect NASH-F. Cut-off values were determined for optimal accuracy, 90% sensitivity and 90% specificity to predict both NASH (PPV 0.732 and NPV 0.668; PPV 0.603 and NPV 0.806; PPV 0.831 and NPV 0.628, respectively) and NASH-F (PPV 0.753 and NPV 0.693; PPV 0.601 and NPV 0.810; PPV 0.838 and NPV 0.649, respectively).

Conclusions : The microsomal liver function of patients with NASH is significantly decreased even in the absence of fibrosis highlighting the sole impact of steatohepatitis on patients' health. The ABT is a valuable tool in assessing the presence of non-fibrotic and fibrotic NASH; and could therefore be used as a supplementary diagnostic tool in clinical practice.

- A04 -

ENDOTHELIN A RECEPTOR ANTAGONIST BQ-123 AND ANGIOTENSIN RECEPTOR BLOCKER VALSARTAN ATTENUATES THE INCREASED TRANSHEPATIC PRESSURE GRADIENT IN A RAT MODEL OF SEVERE STEATOSIS. D. van der Graaff (1), W. Kwanten (1), J. De Man (1), B. De Winter (1), P. Michielsen (2), S. Francque (2) / [1] Laboratory of Experimental Medicine and Pediatrics, University of Antwerp, Antwerp, Belgium, Department of gastroenterology and hepatology, [2] Universiteit Antwerpen / Antwerp University Hospital, Wilrijk (Antwerpen), Belgium, Department of gastroenterology and hepatology.

Introduction : Non-alcoholic fatty liver disease (NAFLD) has become the most prevalent chronic liver disease of the Western world. Prior to the development of inflammation or fibrosis, the intrahepatic vascular resistance (IHVR) is increased both in animals and in patients, impairing hepatic blood flow and potentially causing tissue hypoxia and disease progression. Changes in the endothelin-1 (ET-1) and the angiotensin II (ATII) pathways are potential underlying mechanisms.

Aim : The aim was to elucidate the role of ET-1 and ATII in the IHVR in an animal model of severe steatosis without inflammation or fibrosis.

Methods : The IHVR was studied by measuring the transhepatic pressure gradient (THPG) in an in situ ex vivo rat perfusion model, in which the liver is isolated, connected to a circuit with a pump and perfused by Krebs solution with the addition of drugs or placebo (Krebs). The THPG was studied in Wistar rats (n=7-8/group) on a methionine-choline-deficient diet, inducing severe steatosis after 4 weeks, and compared to rats on a control diet. The effects of ET-1 (10^{-12} - 3×10^{-10} M) and ATII (3×10^{-9} - 10^{-6} M) were tested in dose-response experiments, in which the dose was increased by 0.5 log M every 5 minutes at a constant flow of 30 mL/min. Next, the effects of BQ-123 (ETA-receptor antagonist, 1.3 - 400×10^{-9} M) and BQ-788 (ETB-receptor antagonist, 0.12 - 36×10^{-9} M) were studied in dose-response experiments in the presence of 10^{-10} M ET-1 at a constant flow of 30 mL/min. Valsartan (VAL, 0.2×10^{-6} - 60×10^{-6} M), an ATII receptor blocker, was tested in a dose-response experiment in the presence of 10^{-8} M ATII at a constant flow of 30 mL/min.

Results : ET-1 induced a dose-dependent increase of the THPG in both controls and steatosis, with significantly increased sensitivity and responsiveness to ET-1 in steatosis (20.3 ± 1.3 mmHg at 3×10^{-10} M, 280.6% increase from baseline) compared to controls (14.9 ± 1.4 mmHg at 3×10^{-10} M, 179.2% increase from baseline, $p < 0.001$). In control liver, blocking the ETA-receptor induced a significant decrease in THPG compared to Krebs, most evident at 400×10^{-9} M BQ-123 (13.6 ± 1.0 mmHg with Krebs vs. 10.3 ± 0.7 mmHg with BQ-123, 24.3% decrease). In steatotic liver, the THPG decreased more profoundly after blocking the ETA-receptor (24.9 ± 4.5 mmHg with Krebs vs. 16.1 ± 1.1 mmHg with 400×10^{-9} M BQ-123, 35.4% decrease), to a level comparable to control liver. Blocking the ETB-receptor, however, did not show any change in the THPG in controls nor steatosis. ATII induced an initial increase of the THPG with a maximum effect at 10^{-8} M, and subsequently a gradual decrease of the THPG at increasing doses both in controls and in steatosis (controls: 12.6 ± 1.7 with 10^{-8} M ATII, 187.4% increase from baseline; steatosis: 16.6 ± 2.0 mmHg with 10^{-8} M ATII, 199.6% increase from baseline). When the ATII receptor was blocked by VAL, the THPG and the angiotensin-induced peak were decreased (controls: 15.0 ± 0.4 mmHg with ATII to 12.8 ± 0.6 mmHg with ATII and VAL; steatosis: 18.6 ± 0.6 mmHg with ATII to 16.9 ± 0.8 mmHg with ATII and VAL). Interestingly, the THPG in steatosis with VAL decreased to the THPG of control livers without VAL from a dose of 6×10^{-6} M and higher (controls 10.1 ± 0.7 mmHg with ATII, steatosis 9.6 ± 0.4 mmHg with ATII and 6×10^{-6} M VAL, $p = 0.8$).

Conclusions : The reactivity to ET-1 was significantly increased in steatotic livers compared to controls and appeared to be ETA-receptor mediated. Blocking the ETA receptor or the angiotensin II receptor normalised the increased transhepatic pressure gradient in severe steatosis. Therefore, these pathways seem to be involved in the increased IHVR in NAFLD and could potentially be interesting therapeutic targets in the treatment of NAFLD.

- A05-

COMBINATION OF UBIQUITIN CARBOXY-TERMINAL HYDROLASE L1 INHIBITION AND SORAFENIB TREATMENT IN EXPERIMENTAL HEPATOCELLULAR CARCINOMA DAMPENS TUMOR AGGRESSIVENESS AND REDUCES IN VITRO FUNCTIONAL LIVER CANCER STEM CELL CHARACTERISTICS. A. Vandierendonck (1), L. Devisscher (2), G. Lerno (1), E. Van De Vijver (1), H. Degroote (3), B. Vanderborcht (1), S. Van Campenhout (1), S. Lefere (3), Y. Vandewynckel (3), C. Ampe (4), M. Van Troys (4), H. Van Vlierberghe (3). [1] Ghent University, Ghent, Belgium, Dpt. Gastroenterology and Hepatology, [2] Ghent University, Ghent, Belgium, Dpt. Basic and Applied Medical Sciences, [3] University Hospital Gent, Belgium, Dpt. Gastroenterology and Hepatology, [4] Ghent University, Ghent, Belgium, Dpt. Biochemistry.

Introduction : Hepatocellular carcinoma (HCC) is the second leading cause of cancer-related mortality worldwide. In the majority of patients with advanced HCC, therapy with the golden standard sorafenib (SFN) has limited efficacy with frequent adverse events and often results into aggressive relapse. It has been put forward that liver cancer stem cells (LCSC) play a pivotal role in therapy resistance, invasion, metastasis, and recurrence of HCC. Consequently, treatment strategies combining SFN with targeted compounds to potentially diminish LCSC properties are an unmet medical need. Ubiquitin carboxy-terminal hydrolase L1 (UCHL1) is a key regulator of protein homeostasis and has been reported to be deregulated in HCC. However, its role as a tumor promoter or suppressor remains controversial.

Aim : In this study, we investigated the potential of the UCHL1 inhibitor LDN57444 (LDN) on functional stemness features compared to and in combination with SFN treatment.

Methods : Orthotopic multifocal HCC in mice was established by N-nitrosodiethylamine (DEN) injections for 25 weeks. Ectopic human HCC xenografts were obtained by subcutaneous injection of 5×10^6 human Hep3B cells in nude mice. Animals were treated with 10 mg/kg SFN (daily), 0.4 mg/kg LDN (biweekly), combined therapy or vehicle

for 5 or 3 weeks (DEN or xenograft model, respectively). Expression of HCC markers was evaluated in ectopic and orthotopic tumors, and corresponding non-neoplastic liver tissue by RT-qPCR. Tumor cell proliferation and viability were assessed by histological analyses (Ki-67 and H&E) of the ectopic tumors and validated in vitro by MTT and LDH assays. Assessment of functional LCSC characteristics was performed in vitro by colony formation and 3D spheroid invasion assays with SFN, LDN or combined treatment.

Results : Although no significant differences in tumor burden (DEN model) or volume (xenograft) were observed, similar survival benefits and reduction of intra-tumoral HCC marker expression was observed in ectopic and orthotopic HCC mice treated with SFN or the combination therapy. Xenograft tumors were less aggressive upon combination therapy, with reduced numbers of proliferative Ki-67 positive cells and enhanced necrotic tumor centers. This was confirmed in vitro with significant loss of viability and cell integrity in Hep3B cells treated with both SFN and LDN compared to cells treated with SFN or LDN alone. Interestingly, combo-treated cells displayed less functional LCSC features shown by reversed SFN-induced colony formation and strongly reduced spheroid invasiveness in collagen matrix.

Conclusions : Combination of UCHL1 inhibition and SFN treatment in HCC mice dampens tumor aggressiveness. Inhibiting UCHL1 in SFN-treated HCC cells reduces functional LCSC characteristics. Further in vivo studies using a metastatic HCC xenograft model will be used to establish whether this strategy is able to subdue HCC metastasis.

- A06 -

COMBINATION OF GLYCYRRHIZIN AND N-ACETYLCYSTEINE: BENEFIT OUTCOME IN A MURINE MODEL OF ACETAMINOPHEN-INDUCED LIVER FAILURE. C. Minsart (1), S. Rorive (2), E. Quertinmont (3), A. Lemmers (4), T. Gustot (4) / [1] Université Libre de Bruxelles Faculté de Médecine, Brussels, Belgium, Laboratoire de Gastroentérologie Expérimentale, [2] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Pathology, [3] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Laboratory of Experimental Gastroenterology, [4] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Gastroenterology, HepatoPancreatology and Digestive Oncology.

Introduction : Acetaminophen overdose is the most frequent cause of drug-induced liver failure in the developed countries. Despite substantial progress in the understanding of the mechanism of hepatocellular injury, N-acetylcysteine remains the only effective treatment if administered within 8 to 10 hours of ingestion of the overdose. Thus, other hepatoprotective drugs are needed for the delayed treatment of acetaminophen-induced hepatotoxicity. Glycyrrhizin, an aqueous extract of licorice root, is also known to have hepatoprotective effects.

Aim : This study aimed to investigate the efficacy of the combination of glycyrrhizin and N-acetylcysteine compared to N-acetylcysteine alone in the prevention of liver toxicity in a murine model of acetaminophen-induced liver injury.

Methods : Mice fasted for 15h were treated with acetaminophen (500mg/kg) by intraperitoneal injection and separated into following groups: glycyrrhizin (200mg/kg), N-acetylcysteine (150mg/kg) and glycyrrhizin/N-acetylcysteine. In all groups, mice were sacrificed 12h following acetaminophen administration. Haematological analyses, histopathological parameters and survival rates were compared between various groups.

Results : Consistent with earlier data, intraperitoneal administration of acetaminophen in mice induced a severe liver injury characterized by release of alanine aminotransferase and centrilobular hepatocyte necrosis. Treatment with glycyrrhizin, N-acetylcysteine or N-acetylcysteine/glycyrrhizin combination, at the same time of acetaminophen, decreased significantly alanine aminotransferase levels and necrosis score. At this stage, the N-acetylcysteine/glycyrrhizin combination was as effective as N-acetylcysteine alone. Delayed administration, two hours or six hours after acetaminophen challenge, induced significant decrease of hepatocytes necrosis in group of mice treated with N-acetylcysteine/glycyrrhizin combination ($p < 0,01$) compared to other groups. Furthermore, the administration of N-acetylcysteine/glycyrrhizin combination was found to be associated with better survival rates. The results showed that treatment with N-acetylcysteine/glycyrrhizin combination prevented significantly ($p < 0,001$) mice mortality compared to N-acetylcysteine alone. Potential interference, between N-acetylcysteine/glycyrrhizin treatment and acetaminophen metabolism, was evaluated and we have not demonstrated significantly differences between groups of mice.

Conclusions : Compared with N-acetylcysteine given alone, concomitant administration of glycyrrhizin decreased the liver necrosis score and improved the survival during acetaminophen-induced liver injury in mice. These results suggest for the first time that the combination of an antioxidant like N-acetylcysteine and an anti-inflammatory drug like glycyrrhizin prevented the liver damage induced by acetaminophen intoxication.

- A07 -

PORTAL VEIN THROMBOSIS IN PATIENTS ON THE WAITING LIST FOR LIVER TRANSPLANTATION: A SINGLE CENTER COHORT STUDY. J. Bert (1), A. Geerts (1), A. Vanlander (2), L. Abreu De Carvalho (2), F. Berrevoet (2), R. Troisi (2), X. Rogiers (2), H. Van Vlierbergh (1), X. Verhelst (3) / [1] Ghent University Hospital, Ghent, Belgium, Gastroenterology and Hepatology, [2] Ghent University Hospital, Ghent, Belgium, General and Hepatobiliary Surgery, [3] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology and Hepatology.

Introduction : Portal vein thrombosis (PVT) is a well-recognized complication of end-stage liver disease. However, current literature is still inconclusive about its impact on the clinical course in liver transplant candidates.

Aim : The aim of this study was to identify the prevalence of and the risk factors for PVT, to assess the usefulness of anticoagulant therapy and to determine the impact of thrombosis as well as anticoagulation on postoperative outcomes, patient and graft survival.

Methods : We performed a single center retrospective cohort study in an expert liver transplant unit. Patient receiving liver transplantation between January 2006 and June 2016 were included. Relevant demographic, clinical and outcome data were retrieved from the medical records. For analysis, patients were stratified in two groups according to presence of PVT. Univariate and multivariate logistic regression analysis and survival analysis were performed.

Results : During the study period 390 adult patients underwent orthotopic liver transplantation. In 40 patients (10,26%) PVT was diagnosed. In respectively 10 (2,56%), 7 (1,79%) and 23 (5,9%) patients, the thrombus was identified at time of evaluation for transplantation, during waiting time and at time of transplantation. Among the 37 (9,49%) cases who still had PVT at the time of transplantation, 20 (54,05%) showed partial and 17 (45,05%) showed complete thrombosis. In a multivariate analysis, body mass index ($p=0,006$; OR 1,1; 95% CI:1,028-1,177), previous treatment of portal hypertension ($p=0,001$; OR 3,59; 95% CI:1,681-7,671) and a history of encephalopathy ($p=0,007$; OR 2,86; 95% CI=1,332-6,142) were independently associated with the occurrence of PVT. A beneficial trend was present favouring the use of anticoagulation towards the accomplishment of recanalization ($n=3/7$ versus $0/9$; $p=0,062$). In the anticoagulated patients, only one mild bleeding episode (14,3%) occurred. Operation time was increased ($p=0,001$) in patients where the thrombus was discovered incidentally during surgery. Length of stay was increased ($p=0,012$) in the presence of PVT. Patient and graft survival rates were similar between the groups with and without portal vein thrombosis after 5 year of follow up. However, 1-year patient survival was significantly lower ($p=0,031$) in patients with PVT. Variables independently associated with the risk of 1-year and overall patient mortality included respectively the presence of portal vein thrombosis ($p=0,032$) and male gender ($p=0,023$).

Conclusions : PVT occurred in 10% of patients awaiting liver transplantation and had a deleterious effect on one year survival after liver transplantation. Anticoagulation is safe and showed a beneficial trend on recanalization of PVT and on the one year survival rate.

- A08 -

THE GENE SIGNATURE-MELD SCORE AND ALCOHOL CONSUMPTION DETERMINE LONG-TERM PROGNOSIS OF PATIENTS WITH SEVERE ALCOHOLIC HEPATITIS. P. Deltenre (1), E. Trépo (2), N. Fujiwara (3), N. Goossens (4), A. Marot (5), M. Dubois (6), L. Spahr (4), J. Henrion (7), C. Moreno (2), Y. Hoshida (3) / [1] Clinique Saint-Luc Bouge, Namur, Belgium, Division of Gastroenterology and Hepatology, [2] C.U.B. Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium, Department of Gastroenterology, Hepatopancreatology, and Digestive Oncology, [3] University of Texas Southwestern Medical Center, Dallas, United States (the), Division of Digestive and Liver Diseases. Department of Internal Medicine, [4] Geneva University Hospital, Geneva, Switzerland, Division of Gastroenterology and Hepatology, [5] CHU UCL Namur, Yvoir, Belgium, Department of Gastroenterology and Hepatology, [6] Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland, Division of Gastroenterology and Hepatology, [7] Hôpital de Jolimont, Haine-Saint-Paul, Belgium, Department of Gastroenterology and Hepatology.

Introduction : Accurate prediction of long-term prognosis of patients with severe alcoholic hepatitis (AH) is mandatory to guide therapeutic strategy. The gene signature-MELD (gs-MELD) score, a combination of a gene signature and the MELD score, has been proposed as a new prognostic tool and showed better diagnostic accuracy than all other prognostic scores for assessing the risk of death at 6 months (Trepo et al. Gastroenterology 2018;154:965-75).

Aim : To assess the long-term prognostic value of the gs-MELD score among patients with severe AH.

Methods : Patients with severe AH (Maddrey Discriminant Function >32) treated with methylprednisolone orally at a dose of 32 mg/day for a maximum of 28 days were followed for 5 years from the date of corticosteroid therapy initiation. The primary endpoint was survival at 5 years. The gs-MELD score was generated as described previously. Patients with a gs-MELD greater than 2.66 were considered to have a poor prognosis. Patients were considered abstinent if they had no alcohol consumption during follow-up.

Results : 48 consecutive patients with histologically proven severe AH from 4 European centers were included (median age: 52 years [95% CI: 48-56], median Maddrey Discriminant Function: 50 [95% IC: 45-58]). None had active infection at the start of corticosteroids. Median gs-MELD score was 2.6 (95% CI: 2.2-3.0). 14 (30%) were considered non-responders to corticosteroids at day 7 according to the Lille score. During follow-up, 19 patients (40%) were abstinent, 24 (55%) died and 4 (8%) underwent a liver transplantation. At 5 years, rates of survival without death or liver transplantation were 57% (95% CI: 36-78) and 14% (95% CI: 0-30) in patients with favorable and with poor gs-MELD score ($p<0.001$), and 61% (95% CI: 35-86) and 22% (95% CI: 6-39) in abstainers and in consumers ($p=0.001$), respectively. In time-dependent multivariable proportional hazards models, the gs-MELD score (hazard ratio: 5.78, 95% CI:2.17-15.38, $p<0.001$) and alcohol consumption (hazard ratio: 12.18, 95% CI:3.16-46.95, $p<0.001$) were independently associated with 5-year mortality.

Conclusions : While only the gs-MELD score determines prognosis at short-term, both gs-MELD score and alcohol consumption are independently associated with the risk of death at 5 years. Therapeutic strategies should target alcohol consumption to improve long-term prognosis.

- A09 -

CIRRHOTIC CARDIOMYOPATHY DOES NOT AFFECT OUTCOME IN LIVER TRANSPLANTATION CANDIDATES. E. Vander Straeten (1), I. Colle (1), M. De Pauw (2), A. Geerts (1), X. Verhelst (1), A. Vanlander (3), F. Berrevoet (3), L. Abreu De Carvalho (3), R. Troisi (3), X. Rogiers (3), H. Van Vlierberghe (1), S. Raevens (1) / [1] University Hospital Gent, Belgium, Department of Gastroenterology and Hepatology, Ghent University, [2] University Hospital Gent, Belgium, Department of Cardiology, Ghent University, [3] University Hospital Gent, Belgium, Department of General, Hepatobiliary and Liver Transplantation Surgery, Ghent University.

Introduction : Cirrhotic cardiomyopathy (CCMP) is a chronic cardiac dysfunction in patients with liver disease, in the absence of a known heart disease. CCMP is defined as diastolic dysfunction (DD) and/or systolic dysfunction (SD). Diagnostic criteria were first established in Montréal in 2005. However, with the application of tissue Doppler imaging, the evaluation of DD has substantially evolved, and thus, former criteria may be obsolete. Furthermore, data on the prognosis of CCMP and its clinical impact, especially with regard to liver transplantation (LT) and post-LT outcome, are sparse.

Aim : In this retrospective study, we applied different sets of diagnostic criteria for DD and SD to a patient population of LT candidates, and aimed to estimate the prevalence of CCMP. We analysed the influence of DD, SD and CCMP on overall, pre- and post-LT outcome. In addition, the reversibility of DD and SD post-LT was examined. Lastly, we tested whether echocardiographic parameters can predict post-LT mortality.

Methods : Demographic, clinical, echocardiographic and outcome data of 312 adult patients on the waitlist for LT between 01/01/2011 and 31/03/2017 in the Ghent University Hospital were retrospectively studied. We applied the criteria for DD and SD, described in the Montréal consensus, ASE/EAE 2009, ASE/EACVI 2015/2016 and Thoraxcenter 2016, to our study population to estimate the prevalence of CCMP. Next, we used the ASE/EACVI 2016 criteria (based on e' septal, e' lateral, mean E/e' and TR velocity) to study the clinical impact of DD. For SD, we used the ASE/EACVI 2015 criteria (based on ejection fraction). Data were analysed using SPSS Statistics Version 24.

Results : Echocardiographic parameters were available in 140 patients. According to the Montréal consensus the prevalence of DD was 76%, SD 2% and CCMP 80%. The used criteria are however very broad, non-specific and can be considered outdated. The prevalence of DD was 24% according to Thoraxcenter. Using the most recent ASE guidelines, which include tissue Doppler imaging measurements, the prevalence of DD was 6% (9/157), SD 1% (2/201) and CCMP 7% (10/140). All patients with DD had moderate disease. 1 patient had moderate SD and 1 patient had moderate-severe SD. The presence of DD, SD or CCMP did not affect pre-LT outcome (P=0.37): 30% (3/10) patients with CCMP died on the waitlist vs 12% (16/130) patients without CCMP. 70% (7/10) patients with CCMP underwent LT vs 84,6% (110/130) patients without CCMP. Patients were followed for a mean period of 3 years and 10 months post-LT. Post-LT survival was similar in both groups: 85,7% (6/7) in the CCMP group and 84,5% (93/110) in the non-CCMP group (P=1). 80% (4/5) of transplanted patients with DD no longer had evidence of DD after LT. However, 2 patients without DD pre-LT developed DD after transplantation. Statistical analysis indicated that (history of) smoking (OR 95%CI: 1,8–7,9, P=0,001), pulmonary comorbidities (OR 95%CI: 1,3–5,4, P=0,006), hyponatremia (OR for increasing sodium, 95% CI: 0,89–0,99 (P=0,027) and increased severity of liver disease (OR for Child-Pugh score, 95%CI 1,1-1,4, P=0,001) are associated with worse clinical outcome on the waitlist. Predictors for post-LT mortality were cardiac comorbidities (OR 95%CI: 1,2–5,9, P=0,019) and increased RVEDD/LVEDD (OR 95%CI: 1,1–4413,6, P=0,046). Other echocardiographic parameters do not seem to be useful to predict waitlist or post-LT outcome.

Conclusions : According to most recent cardiology guidelines, the prevalence of CCMP among LT candidates is rather low, 7%. Our results indicate that the presence of CCMP does not affect waitlist outcome or post-LT survival.

- A10 -

SEVERITY OF NAFLD IS ASSOCIATED WITH BOTH MORE SEVERE β -CELL DYSFUNCTION AND REDUCED INSULIN CLEARANCE INDEPENDENTLY OF BODY WEIGHT IN A LARGE COHORT OF NON-DIABETIC SUBJECTS: FURTHER INSIGHTS IN THE CAUSATIVE ROLE OF NASH IN T2DM DEVELOPMENT. L. Vonghia (1), F. Carli (2), A. Verrijken (3), J. Weyler (1), E. Dirinck (3), P. Michielsen (1), T. Vanwolleghem (1), A. Driessen (4), L. Van Gaal (3), A. Gastaldelli (2), S. Francque (1) / [1] Antwerp University Hospital, Antwerp, Belgium, Edegem, Belgium, Department of Gastroenterology and Hepatology, [2] Institute of Clinical Physiology, CNR, Pisa, Italy, Pisa, Italy, Cardiometabolic Risk Unit, [3] Antwerp University Hospital, Antwerp, Belgium, Edegem, Belgium, Department of Endocrinology, Diabetology and Metabolism, [4] Antwerp University Hospital, Antwerp, Belgium, Edegem, Belgium, Department of Pathology.

Introduction : Patients with non-alcoholic fatty liver disease (NAFLD) are at high risk to develop type 2 diabetes (T2DM). It is well established that β -cell dysfunction, i.e. impairment in insulin secretion meant to overcome the muscle insulin resistance (IR), is a strong predictor of the development of postprandial hyperglycemia and T2DM. The liver plays a central role since it clears up to 80% of the secreted insulin. However, in conditions of liver disease and/or IR the insulin clearance (ClearIns) is reduced.

Aim : The goal of this study was to evaluate if insulin secretion rate (ISR) and β -cell function were decreased in Non-alcoholic steatohepatitis (NASH) vs Non-alcohol Fatty Liver (NAFL) thus predisposing these subjects to T2DM.

Methods : We analyzed the glucose, insulin and c-peptide profiles (at 0,30,60,120,180min) during a 75gram oral glucose tolerance test (OGTT) in 402 non-diabetic NAFLD patients (BMI kg/m 25-69, age 18-74 years, 31.5/68.4% M/F). We assessed Matsuda insulin sensitivity index (ISI), ISR during OGTT (from deconvolution analysis of c-peptide), the insulin response to glucose (Δ AUC-I/ Δ AUC-G) and ClearIns. We also determined β -cell function as the insulin secretion/insulin resistance or disposition index (DI) (i.e. calculating the insulin response factored by the degree of IR: $DI=ISI \cdot \Delta$ AUC-I/ Δ AUC-G). A low DI was used to indicate a predisposition to develop T2DM. Liver biopsy was scored according to NASH CRN. In this cohort n=224 patients had NASH.

Results : Subjects were grouped according to liver histologic phenotype as NAFL, NASH with low or high fibrosis (NASH-LF vs NASH-HF) and according to BMI as non-obese (BMI<30), obese (BMI 30-40) or morbid obese (BMI>40). Obesity was associated with increased IR, fasting and postprandial insulin secretion, but decreased ClearIns. Within each weight category, NAFLD severity was significantly associated with increased IR, ISR and decreased ClearIns. β -cell function assessed by DI was significantly decreased with both severity of liver disease and obesity.

Conclusions : β -cell dysfunction is more prevalent in non-diabetic obese subjects and is significantly aggravated by the concomitant presence and severity of NAFLD supporting an independent causative role of NAFLD in development of T2DM. Furthermore, insulin clearance is even so decreased in relation to the presence and severity of NAFLD.

- A11 -

ORAL VASODILATOR TREATMENT AND LIVER TRANSPLANTATION FOR PORTOPULMONARY HYPERTENSION: SYSTEMATIC REVIEW AND META-ANALYSIS OF HEMODYNAMIC RESPONSE AND PROGNOSIS. R. Deroo (1), M. De Pauw (2), E. Trépo (3), T. Holvoet (4), A. Geerts (4), X. Verhelst (4), I. Colle (4), H. Van Vlierbergh (4), S. Raevens (4) / [1] Ghent University Hospital, Ghent, Belgium, Gastroenterology and Hepatology, [2] Ghent University, Ghent, Belgium, Cardiology, [3] C.U.B. Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium, Gastroenterology, Hepatopancreatology and Digestive Oncology, [4] Ghent University Hospital, Ghent, Belgium, Gastroenterology and hepatology.

Introduction : Portopulmonary hypertension (PoPH) is a severe complication of portal hypertension. Historical data indicate that untreated PoPH carries very poor prognosis. Although liver transplantation (LT) may lead to resolution of PoPH, advanced stages may jeopardize a safe procedure. Oral vasodilator (VD) drugs are used to lower pulmonary pressure, and may serve as a bridge to LT. Current use of pulmonary pressure reducing agents comes from trials in pulmonary arterial hypertension. Occasional small single center reports have described the use of oral VD drugs, followed or not by LT, to improve pulmonary pressure and functional status in patients with PoPH. However, no study has systematically summarized the reported effects on pulmonary hemodynamic response, LT eligibility, and prognosis in this patient population.

Aim : The aims were to provide summary estimates on pulmonary hemodynamics and survival in patients with PoPH, treated with (1) oral VD therapy, (2) oral VD therapy followed by LT, or (3) no intervention. Also, we aimed to define to which extent VD therapy allows LT eligibility, and whether VD treatment can be weaned post-LT.

Methods : We performed a systematic review with meta-analysis of observational cohort and case-control studies describing no treatment, medical intervention or LT in patients with PoPH. Relevant publications up to July 1, 2018 in English were searched in PubMed, Web of Sciences, and Embase. Observational cohort studies reporting on ≥ 5 PoPH cases were included. Studies had to: a) include adult (≥ 18 years of age) PoPH patients, in whom the diagnosis was made based on right heart catheterization measurements, who were either not treated or treated with VD agents and/or LT; b) provide follow-up data relative to survival and pulmonary hemodynamics. Both single-arm studies and studies including different treatment groups were included. Pooled estimates and 95% confidence intervals (CI) were calculated using a random effects model.

Results : Twenty-six studies (n=1088 patients) were included. 39% of patients had Child-Pugh A. Most common causes of portal hypertension were alcoholic (44%) and viral (25%) liver disease. Overall, VD only therapy decreases the mean pulmonary artery pressure (mPAP) by 9.6 mmHg (CI: - 13.6,-5.6) and pulmonary vascular resistance (PVR) by 241 dyne.s.cm-5 (CI: -281.7,-200.7). A substantial proportion of patients treated with VD becomes eligible for LT (pooled estimate 45%, CI: 32-60). VD combined with LT decreases mPAP by 11.9 mmHg (CI: - 18.7,-5.1) and PVR by 184 dyne.s.cm-5 (CI: -256.7,-112.1). Pooled estimates for 1-year, 3-year, and 5-year survival after diagnosis in patients treated with VD were 86% (CI: 83-90), 66% (CI: 53-78), and 49% (CI: 36-62) respectively. Pooled estimates for 1-year, 3-year and 5-year survival after diagnosis in patients undergoing LT who were pretreated with VD were 82% (CI: 52-

95), 67% (CI: 53-78) and 69% (CI: 43-86) respectively. Pooled estimates for 1-year and 3-year survival after LT were 78% (CI: 69-85) and 75% (CI: 68-80). Overall, the pooled estimate for death was 62% (CI: 40-81) in patients who were not treated, 34% (CI: 25-45) in patients treated with VD, 36% (CI: 21-53) in patients who underwent LT and 22% (CI: 15-31) in patients who underwent LT after they had been pretreated with VD. Nine studies (410 patients) included both patients who received VD only and patients who received VD followed by LT, enabling direct comparison between the two groups. The risk of death in VD-only-treated patients was significantly higher than in patients who were transplanted too (odds ratio 2.45; CI: 1.141, 5.239). A significant number of deaths in patients with PoPH are caused by progressive pulmonary hypertension and right heart failure: 34% (CI: 12-56) in the VD group and 55% (CI: 35-73) in the LT group. Interestingly, 48% of patients was able to discontinue VD therapy post-LT (CI: 37-60).

Conclusions : Oral VD therapy and VD therapy followed by LT improve pulmonary hemodynamics and prognosis in patients with PoPH. In cases where LT is considered safe and feasible, the combination of VD therapy confers a better prognosis than medical treatment only.

- A12 -

NEW CONCEPTS IN LIVER REGENERATION MECHANISMS IN HUMAN SEVERE ALCOHOLIC STEATOHEPATITIS. A. Lejeune (1), P. Stärkel (1), A. Louvet (2), A. Hittelet (3), C. Bazille (4), B. Bastens (5), H. Orlent (6), L. Lasser (7), X. Dekoninck (8), S. Negrin-Dastis (9), J. Delwaide (10), A. Geerts (11), C. de Galocsy (12), V. Putzeys (13), P. Langlet (14), H. Reynaert (15), S. Francque (16), M. Komuta (17), N. Lanthier (1) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'Hépatogastroentérologie, [2] Hôpital Huriez, Lille, France, Service des Maladies de l'Appareil Digestif, [3] Hôpital Ambroise Paré, Mons, Belgium, Department of Gastroenterology, [4] Centre Hospitalier Universitaire de Caen, Caen, France, Service d'Anatomie Pathologique, [5] Hôpital Saint-Joseph, Liège, Belgium, Department of Gastroenterology, [6] Academisch Ziekenhuis Sint-Jan, Brugge, Belgium, Department of Gastroenterology and Hepatology, [7] Centre Hospitalier Universitaire Brugmann, Brussels, Belgium, Department of Hepatogastroenterology, [8] Clinique Saint-Pierre, Ottignies, Belgium, Department of Gastroenterology, [9] Clinique Saint-Joseph, Mons, Belgium, Department of Gastroenterology, [10] Centre Hospitalier Universitaire Sart-Tilman, Liège, Belgium, Department of Hepatogastroenterology, [11] Ghent University Hospital, Ghent, Belgium, Department of Hepatogastroenterology, [12] Hôpitaux Iris Sud, Brussels, Belgium, Department of Gastroenterology, [13] CHR La Citadelle, Belgium, Department of Gastroenterology, [14] Centre Hospitalier Interrégional Edith Cavell, Brussels, Belgium, Department of Gastroenterology, [15] Universitair Ziekenhuis Brussel, Brussels, Belgium, Department of Hepatogastroenterology, [16] Antwerp University Hospital, Antwerpen, Belgium, Department of Gastroenterology and Hepatology, [17] Cliniques universitaires Saint-Luc, Brussels, Belgium, Department of Pathology.

Introduction : Severe alcoholic steatohepatitis is a severe complication of alcoholic liver disease associated with high mortality. The prediction of patient's outcome remains challenging. Liver progenitor cells (LPC) are usually considered to be activated in case of impaired hepatocyte replication and hence markers of disease severity. However, their exact role as well as their interaction with hepatocytes and macrophages also implicated in liver regeneration remain poorly characterized in humans.

Aim : The aim of this study is to characterize hepatocyte, LPC and macrophage populations in severe alcoholic steatohepatitis (sASH) and to link them with liver injury and patients' outcomes.

Methods : The material used for this study is derived from the recent trial on enteral nutrition in severe biopsy proven alcoholic steatohepatitis, including initially 136 patients. Immunohistochemical and morphometric studies for total LPC (keratin 7 positive cells), macrophages (CD68 positive cells), proliferative hepatocytes (Ki67 positive hepatocytes) and proliferative LPC (double keratin 7 positive and Ki67 positive cells) were performed on the admission biopsies of patients with sASH recruited prospectively in several different centers in Belgium and France. Patients were divided into improvers or non-improvers, according to MELD score change (a decrease of at least 3 points of MELD or more compared to baseline value defines improvers) and in responders or non-responders to corticosteroids, according to the Lille score at day 7.

Results : Liver biopsies were available for 68 patients with sASH from 16 different centers. Eleven biopsies were excluded due to the poor quality of the remaining material. 57 cases were included for histological and morphometric assessment (mean age 50 years, mean Maddrey discriminant function 54, range 43.2-71.5). No difference of total LPC, proliferative LPC, proliferative hepatocytes or macrophages was observed between improvers (n=26) and non-improvers (n=31) nor between the favorable (n=43) and unfavorable (n=14) Lille score groups. A greater degree of steatosis was the only histological parameter associated with a better prognosis based on MELD score evolution at 3 months (p=0.002). The total amount of LPC was positively correlated to the severity of the disease evaluated by the MELD score (r=0.3416, p<0.01). A higher number of macrophages was associated with a higher proliferation of both hepatocytes and LPC (r=0.3012, p=0.02). Increased hepatocyte replication was also correlated to a higher proliferative LPC count (r=0.8112, p<0.0001).

Conclusions : In biopsy proven severe alcoholic steatohepatitis, the proliferation of hepatocytes and LPC occurs in parallel, showing that LPC start to replicate even in the absence of massive hepatocyte senescence in humans, which

contrasts with data coming from animal experiments. Liver macrophage expansion is correlated to the proliferation of both hepatocytes and LPC suggesting a potential role for driving the regenerative response.

- A13 -

DOES MUCOSAL INFLAMMATION DRIVE RECURRENCE OF PSC IN LIVER TRANSPLANT RECIPIENTS WITH ULCERATIVE COLITIS? N. Dekkers (1). [1] Leiden University Medical Center (LUMC), Leiden, The Netherlands, Gastroenterology.

Introduction : Primary Sclerosing Cholangitis (PSC) is a progressive fibro-inflammatory disease of the biliary tract. PSC is in 70-80% of the patients associated with inflammatory bowel disease (IBD), mostly ulcerative colitis (UC). A liver transplantation (LT) remains the only effective treatment for a PSC complicated with end-stage liver disease, recurrent cholangitis or therapy-refractory hepatogenic pruritus as no evidence based disease-modifying treatment for PSC is available. However, recurrence of PSC (rPSC) is estimated to re-occur in 11% of patients transplanted for complicated PSC

Aim : This study aimed to assess risk factors of rPSC

Methods : a retrospective cohort study was performed gathering the data of 2 academic referral centers (Leuven, Belgium and Leiden, The Netherlands) on all UC and non-IBD patients that underwent liver transplantation for PSC. Follow-up started at time of transplantation and ended at death, recurrence of PSC or graft failure due to other causes. The following risk factors were assessed: presence and histological activity of UC, coinciding cytomegalovirus (CMV) infections, recipient age at transplant, gender, gender mismatch and age difference between donor and recipient, intercurrent rejection, type of donor-procedure, presence and timing of colectomy, cholangiocarcinoma prior to transplant and drug usage. For the assessment of mucosal inflammation, the histological Geboes score was used

Results : In total, 81 patients with PSC who underwent a liver transplantation were included, of which 62 (76.5%) were diagnosed with UC. Seventeen patients (21.0%) developed rPSC during a median follow-up time of 5.2 years and ten (58.8%) of them experienced graft failure. In a subset of 42 patients no association was found between the degree of mucosal inflammation and rPSC, using both original Geboes scores and multiple cut-off points. In the total cohort, CMV infections post-LT (HR: 4.576, 95% CI 1.688-12.403) and younger receiver age at time of liver transplantation (age at LT: (HR: 0.934, 95% CI 0.881-0.990)) were independently associated with an increased risk of rPSC. rPSC was not associated with an increase in mortality.

Conclusions : In this multicentre retrospective cohort study, no association was found between the degree of mucosal inflammation and rPSC. In contrast, CMV infection post-LT and a younger receiver age at LT are associated with an increased risk of rPSC.

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CONSTRUCTING A PRIMARY MOUSE 3D HEPATIC CO-CULTURE MODEL THAT RECAPITULATES HSC ACTIVATION DURING FIBROSIS. I. Mannaerts (1), N. Eysackers (1), A. Smout (1), S. Verhulst (1), S. Leite (1), T. Roosens (1), L. Van Grunsven (1) / [1] Vrije Universiteit Brussel (VUB), Jette, Belgium, Liver Cell Biology Research Group.

Introduction : Chronic liver disease is the major cause of progressive liver fibrosis which, in turn, leads to cirrhosis of the liver. One major obstacle in the development of efficient therapies is the lack of robust and representative in vitro models of liver fibrosis to aid in understanding the basic mechanisms of the disease and in the development phase of pharmaceuticals.

Aim : The aim of our work is to develop relevant in vitro liver fibrosis models, based on the central hypothesis that liver fibrosis in vitro cannot be studied using only hepatic stellate cells (HSCs)—the main producer of scar tissue during fibrosis—, but requires cultures in which other liver cells (at least hepatocytes) are integrated.

Methods : We describe the generation of co-culture spheroids, using freshly isolated liver cells from mice. Hepatocytes and HSCs were isolated using percoll gradients and UFACS3 respectively. Spheroids were created and cultured in cell repellent plates and analyzed for RNA changes by qPCR and by immunohistochemistry for protein analysis. Cell viability and compound toxicity were determined by Cell Titer Glo assay.

Results : We show that hepatocytes and HSCs are highly pure at the start of culture and maintain their cell-type specific marker expression over a 15-day culture period. During this period there is no major hepatocyte dedifferentiation or HSC activation, characteristics that cannot be obtained by regular 2D cultures. When exposed to TGF β , paracetamol, or thioacetamide, we observe a compound-mediated HSC activation (direct or via hepatocytes) with a pattern similar to the in vivo HSC activation. Importantly, we can use pharmaceuticals with known anti-fibrotic properties, such as Valproic acid and Verteporfin, to reduce HSC activation in response to hepatocyte damage. Finally, genes that are differentially regulated between (2D) in vitro- and in vivo HSC activation, selected from in-house microarray and RNA-Seq data,

show a more in vivo-like behavior upon paracetamol induced damage in spheroid co-cultured stellate cells compared to the classical 2D HSC cultures.

Conclusions : Our hepatocyte-stellate cell spheroids are a robust in vitro model of liver fibrosis. The hepatocytes can metabolize hepatotoxins and promote HSC activation. This model could facilitate the discovery of, or testing for, novel anti-fibrotic compounds as we have indications that our spheroids are a better representation of HSC activation in vivo compared to the more traditional culture models.

- A15 -

POTENT HEPATITIS B CORE-SPECIFIC B CELL RESPONSES ASSOCIATE WITH CLINICAL PARAMETERS IN UNTREATED AND VIRALLY SUPPRESSED CHRONIC HBV PATIENTS.

T. Vanwolleghem (1), Z. Groothuisink (2), K. Kreeft (2), M. Hung (3), N. Novikov (3), A. Boonstra (4) / [1] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology&Hepatology, [2] Erasmus Medical Center, Rotterdam, The Netherlands, Gastroenterology and Hepatology, [3] Gilead Sciences Inc, , United States (the), Biology, [4] Erasmus MC, Rotterdam, Netherlands, Rotterdam, The Netherlands, Gastroenterology and Hepatology.

Introduction : Exhaustion of virus-specific T cells is a hallmark of chronic HBV (cHBV) infections, but the HBV-specific B cell response is less well studied. Previously, we identified B cell-related transcriptomic changes in blood and liver of cHBV patients in different clinical phases.

Aim : We now examined, the number, phenotype and function of HBcAg-specific B cells during cHBV, in comparison to HBsAg-specific B cells.

Methods : Serum and PBMC were obtained from 137 cHBV patients, both untreated (n=114) belonging to different clinical phases as NUC treated (n=23), and 22 healthy HBsAg-vaccinated controls. The phenotype of overall and HBV-specific B lymphocytes was studied by FACS using DyLight650 and DyLight550 dual fluorescently labelled HBsAg and HBcAg in combination with antibodies against CD3, CD10, CD19, CD27, CD21, CD38, and FcRL5. In vitro anti-HBs and anti-HBc antibody production was measured after polyclonal PBMC stimulation by ELISPOT assays. Anti-HBs and anti-HBc antibodies were measured in serum and in supernatant by ELISA.

Results : Serum levels of anti-HBc, but not anti-HBs antibodies associate with the clinical phases of cHBV, characterized by increasing titers in patients with ALT rise ($P<0.0001$). In vitro, a similar profile is seen for the number of spot-forming anti-HBc-producing cells and their levels in the supernatant of these cultures ($P<0.0001$). Also the number of HBcAg-specific B cells in blood followed this pattern ($P=0.0035$). In contrast, HBsAg-specific B cells show no typical numeric or functional changes in cHBV and are vastly outnumbered by HBcAg-specific B cells in blood (92.8-fold, $P<0.0001$). HBcAg-specific B-cells are enriched for a CD21- and CD21+ CD27+ memory B cell profile compared to total B cells (3.6-fold and 2.0-fold, $P<0.0001$ respectively), but demonstrate a less activated phenotype (activation marker CD38: 0.8-fold, $P=0.0017$; inhibitory IgG co-receptor FcRL5: 2.3-fold, $P<0.0001$). Interestingly, complete viral suppression in the NUC cohort, led to reduced numbers of HBcAg-binding B cells and in vitro production of anti-HBc antibodies (all $P<0.05$). For the total chronic HBV cohort, HBV DNA levels positively correlated with in vitro anti-HBc production levels ($r=0.388$, $P=0.0008$) and with the number of HBcAg-binding B cells ($r=0.323$ $P<0.05$).

Conclusions : HBcAg-specific B cells vastly outnumber HBsAg-specific B cells in blood of chronic HBV patients, are enriched for a classical memory B cell phenotype and show no impairment with increasing HBV DNA titers.

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THE CHANGING PATTERN OF CIRRHOSIS: A COMPARISON OF TWO COHORTS DIAGNOSED 15 YEARS APART. E. Kaze (1), O. Descamps (1), J. Henrion (2) / [1] Centre Hospitalier de Jolimont-Lobbès, La Louvière, Belgium, Internal Medicine, [2] Centre Hospitalier de Jolimont-Lobbès, La Louvière, Belgium, Gastroenterology and Hepatology.

Introduction : The epidemiology of cirrhosis is evolving. For more than 20 years, the main causes of cirrhosis in Western Europe have been excessive alcohol consumption and hepatitis C virus (HCV) infection. More recently, nonalcoholic steatohepatitis (NASH) has emerged as an increasing cause of cirrhosis.

Aim : The aim of this study was to describe the changes in the epidemiology of cirrhosis in our region by comparing two cohorts of patients diagnosed 15 years apart.

Methods : From January 1995 to December 2017, 1154 cirrhotic patients who attended the hepatology outpatient clinic of our institution were consecutively enrolled in a registry. From this registry, we extracted two cohorts of patients diagnosed 15 years apart: the cohort C1 (C1), patients diagnosed between 1995 and 1999 (n=197) and the cohort C2 (C2), patients diagnosed from 2010 to 2014 (n= 237). Baseline characteristics and liver-related mortality were retrospectively compared between both cohorts with a three-to seven-year follow-up (end of 2002 for the cohort C1 and end of 2017 for the cohort C2).

Results : This retrospective monocentric study included 197 cirrhotic patients diagnosed between 1995 and 1999 (cohort C1) and 237 cirrhotic patients diagnosed from 2010 to 2014 (cohort C2). In the cohort C2, compared with the cohort

C1, the prevalence of HVC-related cirrhosis decreased (C1: 22% vs C2: 10%, $p < 0,0001$), the prevalence of NASH-related cirrhosis increased (C1: 3% vs C2: 16%, $p < 0,0001$) and liver biopsy was less frequently performed (C1: 65% vs C2: 20% $p < 0,0001$). The prevalence of alcoholic cirrhosis remained similar between the cohorts (C1: 65% vs C2: 67%). For alcoholic patients, the mean age at diagnosis of cirrhosis was significantly higher in cohort C2 than in cohort C1 (C1: 52 ± 11 years vs C2: 57 ± 10 years, $p < 0,0001$). For patients with HCV-related cirrhosis, the mean age of liver-related death was significantly higher in cohort C2 than in cohort C1 (C1: 70 ± 6 years vs C2: 82 ± 3 years, $p = 0,03$). Concerning Nash-related cirrhosis, there was no statistically differences in the analysed data.

Conclusions : Our study confirmed that NASH is an emerging cause of cirrhosis while HVC-related cirrhosis becomes less frequently observed. For alcoholic patients, cirrhosis is diagnosed at a later age probably because they are more aware of the risks of excessive alcohol intake. In regards to patients with HCV-related cirrhosis, the increasing age of liver-related death may be partially explained by progress in the management of liver diseases. Liver biopsy tended to disappear following the development of non-invasive methods of liver fibrosis assessment.

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EVALUATION OF THE PROGNOSTIC VALUE OF HISTOLOGIC PARAMETERS IN SEVERE ALCOHOLIC HEPATITIS. M. Dubois (1), A. Sciara (2), A. Marot (3), C. Sempoux (2), P. Deltenre (4) / [1] Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland, Division of Gastroenterology and Hepatology, [2] Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland, Institute of Pathology, [3] CHU UCL Namur, Yvoir, Belgium, Department of Gastroenterology and Hepatology, [4] Clinique Saint-luc Bouge, Namur, Belgium, Division of Gastroenterology and Hepatology.

Introduction : Alcoholic Hepatitis (AH) Histologic Score (AHHS) has been proposed as a new prognostic tool to assess the risk of death at 3 months in severe AH.

Aim : To study the prognostic value of AHHS and of Laennec system for survival at 3, 6 and 12 months.

Methods : Liver biopsies of patients with severe AH (Maddrey DF > 32) were analyzed independently by 2 pathologists. Fibrosis, neutrophils, bilirubinostasis and megamitochondria were assessed to classify patients into mild, moderate or severe AHHS. Patients with cirrhosis were also classified according to the Laennec system (4A, 4B and 4C) based on fibrous septa thickness and nodules size.

Results : 55 consecutive patients were included (median age: 54 years [95% IC: 50-56], median Maddrey DF: 71 [95% IC: 64-78]). 43 (78%) were treated with corticosteroids. Four patients (8%) were lost to follow-up at 12 months, 24 (44%) died and 1 (2%) underwent liver transplantation. Histologic scoring, available in 53 patients, showed mild AHHS in 3, moderate AHHS in 11 and severe AHHS in 39. 4 patients had no cirrhosis, 7 patients were classified as Laennec 4A, 15 as 4B and 27 as 4C. Survival rates in mild, moderate and severe AHHS were 100%, 64% and 74% at 3 months ($p = 0,5$), 100%, 55% and 69% at 6 months ($p = 0,4$), and 100%, 55% and 49% at 12 months ($p = 0,4$), respectively. In AHHS, fibrosis showed the best interobserver reproducibility (agreement=100%, $K = 1,00$) and a trend for predicting 1-year survival (100% vs. 49% for patients without and with cirrhosis, $p = 0,14$). AHHS AUROC curve for 12-month survival was 63.4% (95% CI: 46.4-75.9, $p = 0,03$), not different from that of other prognostic scores (Child-Pugh score 58.9%, MELD score 65.5%, Lille score 65.5%, p value for all comparisons $\geq 0,5$). When compared to patients with Laennec 4B or 4C, survival rates of patients without cirrhosis or with Laennec 4A were 91% vs. 68% at 3 months ($p = 0,14$), 82% vs. 64% at 6 months ($p = 0,2$) and 73% vs. 48% at 12 months ($p = 0,14$), respectively. In multivariate analysis adjusted for age and for MELD score, AHHS was not associated with 1-year mortality (risk ratio: 1.27, 95% CI: 0.95-1.70, $p = 0,1$). When considering Laennec system instead of AHHS, Laennec 4B or 4C was not associated with increased mortality at 1 year (risk ratio: 3.52, 95% CI: 0.82-15.17, $p = 0,09$).

Conclusions : AHHS has little added value to predict survival in patients with severe AH. The severity of fibrosis seems the histologic parameter with the strongest prognostic value.

- A18 -

PERSISTENCE OF HEPATIC AND ADIPOSE TISSUE ALTERATIONS IN T HELPER 17 CELLS, CD8+ CYTOTOXIC T CELLS AND REGULATORY T CELLS DESPITE METABOLIC AND HISTOLOGICAL IMPROVEMENT UPON DIET REVERSAL IN A HIGH-FAT HIGH-FRUCTOSE MOUSE MODEL OF NAFLD. M. Van Herck (1), L. Vonghia (2), P. Michielsen (2), C. Bridts (3), D. Ebo (3), J. De Man (4), B. De Winter (4), S. Francque (2) / [1] Universiteit Antwerpen / Antwerp University Hospital, WILRIJK (Antwerpen), Belgium, Laboratory of Experimental Medicine and Pediatrics, Division of Gastroenterology and Hepatology, [2] Universiteit Antwerpen / Antwerp University Hospital, WILRIJK (Antwerpen), Belgium, Gastroenterology and Hepatology, [3] Universiteit Antwerpen / Antwerp University Hospital, WILRIJK (Antwerpen), Belgium, Immunology - Allergology - Rheumatology, [4] University of Antwerp, Antwerp, Belgium, Laboratory of Experimental Medicine and Pediatrics, Division of Gastroenterology and Hepatology.

Introduction : Non-alcoholic fatty liver disease (NAFLD) is a multisystem condition in which the liver, adipose tissue and the immune system are involved. T cells form a part of the adaptive immune system and can be subdivided in several subsets with distinct functions. We previously demonstrated that mice with severe NAFLD exhibit elevated hepatic T helper 17 (Th17) cells (CD4+ ROR γ t+), an abundance of visceral adipose tissue (VAT) CD8+ cytotoxic T (Tc) cells and a reduction of VAT regulatory T (Treg) cells (CD4+ CD25+ Foxp3+).

Aim : This study aimed at investigating the potential reversibility of these alterations upon diet reversal.

Methods : Male 8-week old C57BL/6J mice were fed a high-fat high-fructose diet (HFHFD) for 20 weeks. Subsequently, a diet reversal (DR) was performed by substituting the HFHFD with control diet (CD) and continuing the CD for 12 additional weeks. Three control groups were included: mice fed CD for 32 weeks, HFHFD for 20 weeks and HFHFD for 32 weeks. Liver tissue was assessed histologically and the NAFLD Activity Score (NAS) was calculated. T-cell subsets were characterised in liver and visceral tissue (VAT) via flow cytometry. Tc cells were expressed as a percentage of CD45+ CD3+ cells, Th17 and Treg cells as a percentage of CD3+ CD4+ cells. Data are represented as [median (IQR), p-value].

Results : Compared to CD mice, HFHFD-feeding for 20 and 32 weeks confirmed the previous findings of metabolic alterations, NAFLD development, and the associated hepatic and VAT T-cell alterations, specifically an increase in hepatic Th17 cells [1.6% (1.9) vs. 2.9% (2.8) and 5.7% (11.8) resp., p=0.031] and VAT Tc cells [22.3% (11.5) vs. 40.2% (11.5) and 37.7% (6.7) resp., p=0.004], as well as a reduction in VAT Treg cells [37.4% (28.2) vs. 12.3% (8.9) and 8.5% (9.5) resp., p=0.002]. Compared to mice fed HFHFD for 20 and 32 weeks, DR induced weight loss [resp. 47.3g (6.7) and 52.2g (6.6) vs. 39.4g (9.1), p<0.001], a decrease in cholesterol levels [resp. 140 mg/dL (37) and 170 mg/dL (33) vs. 62 mg/dL (16), p<0.001] and a decrease in NAS [resp. 4 (1) and 6 (1) vs. 1 (3), p<0.001]. No significant difference was observed in NAS between CD-fed mice and DR mice (p=0.160). Conversely, the alterations in hepatic and VAT T cell subsets were not affected by DR: hepatic Th17 cell and VAT Tc levels were significantly higher in DR mice compared to CD-fed mice [4.3% (2.2) vs. 1.5% (1.9), p=0.015 and 35.5% (6.5) vs. 22.3% (11.5), p=0.003 resp.], whereas no significant difference existed between the DR group and mice fed HFHFD for 20 and 32 weeks (p=0.594 and p=0.285 resp.). VAT Treg levels were significantly lower in DR mice compared to CD-fed mice [9.3% (7.1) vs. 37.4% (28.2), p=0.003], whereas no difference existed between the DR group and mice fed HFHFD for 20 and 32 wks (p=0.149).

Conclusions : Although diet reversal induced a metabolic and histological normalisation in HFHFD-fed mice, the HFHFD-induced alterations in hepatic Th17 cells, VAT Tc cells and VAT Treg cells were not reversed within a timeframe of 12 weeks. This finding challenges our current understanding of the reversibility of NAFLD-related inflammation upon life style modification.

- A19 -

MANAGEMENT OF DRUG-DRUG INTERACTIONS IN CHRONIC HEPATITIS C PATIENTS TREATED WITH SECOND GENERATION DIRECT ACTING ANTIVIRALS IN BELGIUM. S. Bourgeois (1), J. Mulkay (2), M. Cool (3), X. Verhelst (4), G. Robaey (5), L. Lasser (6), V. Lefebvre (7), I. Colle (8), C. Van Steenkiste (9), J. Decaestecker (10), S. Coulon (11), K. Venken (12), T. Vanwolleghem (13) / [1] ZNA Middelheim, Antwerpen, Belgium, Department of Gastroenterology and Hepatology, [2] CHU Saint-Pierre, Brussels, Belgium, Department of Gastroenterology and Hepatology, [3] AZ Damiaan, Oostende, Belgium, Department of Gastroenterology and Hepatology, [4] UZ Gent, Gent, Belgium, Department of Gastroenterology and Hepatology, [5] Ziekenhuis Oost Limburg (ZOL), Genk, Belgium, Department of Gastroenterology and Hepatology, [6] CHU Brugmann, Brussels, Belgium, Department of Gastroenterology and Hepatology, [7] CHR, Namur, Belgium, Department of Gastroenterology and Hepatology, [8] ASZ, Aalst, Belgium, Department of Gastroenterology and Hepatology, [9] Maria Middelaers Ziekenhuis, Gent, Belgium, Department of Gastroenterology and Hepatology, [10] AZ Delta, Roeselare, Belgium, Department of Gastroenterology and Hepatology, [11] MSD Belgium, Brussel, Belgium, Medical Department, [12] MSD Belgium, Brussel, Belgium, Medical Department, [13] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Department of Gastroenterology and Hepatology.

Introduction : The new generation of oral direct-acting antivirals (DAAs) has transformed the treatment of hepatitis C virus (HCV) infection, demonstrating both high efficacy and high tolerability. However, none of the DAAs are completely free of drug-drug interactions (DDIs), which can significantly alter the drugs' exposure and hence their efficacy and toxicity (Kondili et al., 2017).

Aim : The aim of the study was to describe the use of concomitant medications and the changes made before starting DAA treatment and ultimately assessing prevalence of patients at risk for potential drug-drug-interactions.

Methods : 405 patients were included in an observational study at 11 centers in Belgium from January 2017 till October 2017. Data were collected on patient characteristics, previous and most recent HCV treatment, comorbidities (MedDRA), comedications (ATC code) and changes made in comedications at start of DAA treatment. Patients were treated with one of the following DAAs: elbasvir/grazoprevir (EBR/GZR); ombitasvir/paritaprevir/ritonavir \pm dasabuvir (OBV/PTV/r \pm DSV); sofosbuvir/daclatasvir (SOF/DCV); sofosbuvir/ledipasvir (SOF/LDV); sofosbuvir/velpatasvir (SOF/VEL). Potential clinically relevant DDIs [co-administration of drugs contraindicated (red) or drugs that may require dose

adjustment/closer monitoring (yellow)] were assessed based on information available at www.hep-druginteractions.org for each drug in August 2018. A Fisher exact test was done for overall comparison (p -value ≤ 0.05 was considered significant) and for comparison between different treatment group (10 pairwise tests) Bonferroni multiple testing correction was done (p -value ≤ 0.005 was considered significant).

Results : The median age was 55 [24;90] years, 60.5% were male, 20.5% were cirrhotic and 31.4% had unsuccessfully been treated before. Patients were treated with SOF/VEL (31.1%), EBR/GZR (27.4%), SOF/DCV (26.4%), OBV/PTV/r±DSV (8.4%) or SOF/LDV (6.7%). RBV was added in 28.6% of the patients. Most common comorbidities were arterial hypertension (27.2%), HIV co-infection (22.5%), type 2 diabetes mellitus (14.3%), alcohol or substance abuse (13.3%) and depression (13.1%). Ninety percent of the patients ($n=365$) took comedications, ranging from 1 to 16 per patient. The predominant therapeutic classes were psycholeptics (28.6%), antivirals for systemic use (24.2%), drugs for acid related disorders (21%), agents acting on the renin-angiotensin system (20.5%) and beta blocking agents (17.5%). Of the 365 patients on co-medications, 20.3% of the patients ($n=74/365$) required an adaptation of their comedication; 42% ($n=31/74$) of them had a change in their comedication (i.e. change in dose, timing or frequency, or switch to another drug) and 67% ($n=50/74$) stopped at least one of their comedications. Seven patients (9.5%) had a stopped and a changed comedication. Drugs used for acid related disorders (31%) and antiviral drugs (33%) were most frequently changed prior to DAA treatment. Lipid modifying agents (43%) and drugs for acid related disorders (21%) were most frequently stopped. Modifications to the comedications of patients at the start of their DAA treatment decreased the risk for potential clinically relevant DDIs from 34% (136/405) to 22% (91/405). Patients treated with EBR/GZR (11%); SOF/DAC (19%) and SOF/VEL (22%) were the least exposed to potential clinically relevant DDIs. While patients treated with LDV/SOF and OBT/PTVr/DSV had respectively 44% and 56% chance for potential clinically relevant DDIs during their DAA treatment (overall p -value < 0.0001). Patients treated with SOF/VEL underwent the most adaptations (29%) to their medication scheme compared to patients treated with EBR/GZR (12%) (p -value < 0.0010 – corrected for multiple testing).

Conclusions : In this Belgian population of HCV patients the majority (90%) of the patients took co-medications. In one fifth (20%) of the patients the treating physician modified the patient's comedications prior to the start of their HCV treatment. According to the Liverpool website, 22% of the patients might be exposed to potential clinically relevant DDI's despite a change prior to DAA initiation. This study suggest that physicians are aware of potential DDIs between co-medications and DAAs but that there is still a gap between the clinical practice and the theoretical recommendations.

- A20 -

DISSECTING THE DIFFERENT ROLES OF ORF3 IN HEV SPREAD AND FECAL SHEDDING IN A HUMANIZED MOUSE MODEL. G. Sari (1), X. Yin (2), A. Boonstra (3), Z. Feng (2), T. Vanwolleghem (4)/ [1] Erasmus MC, Rotterdam, The Netherlands, Gastroenterology and Hepatology, [2] The Research Institute, Ohio (Columbus), United States (the), Center for Vaccines and Immunity, [3] Erasmus Medical Center, Rotterdam, The Netherlands, Gastroenterology and Hepatology, [4] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology&Hepatology.

Introduction : Hepatitis E viruses (HEV) are an important enterically transmitted cause of viral hepatitis. The HEV RNA genome is single-stranded, positive-sensed encoding 3 ORFs (ORF1- 3). Although ORF3 has a viroporin structure and is required for viral propagation in macaques, its exact role remains unclear.

Aim : In the present study, we dissect the function of ORF3 via reverse genetics and infectivity studies, both in vitro as in the liver humanized mouse model.

Methods : A genotype 3 HEV strain (Kernow C1, P6) was used as backbone to construct ORF3 mutant viruses. Virus stocks were produced by transfecting in vitro transcripts into Huh-7 (clone S10-3) cells followed by gradient ultracentrifugation to purify intracellular non-enveloped virions. uPA-NOG and TK-NOG mice ($n=15$) were transplanted with human hepatocytes from a single donor and inoculated iv with above mentioned ORF3 mutant viruses (6 log₁₀ geq/mouse) upon establishment of a stable graft. Weekly feces and serum samples were obtained during the 6-weeks infection course, after which animals were sacrificed and liver and bile were collected for viral load determination by multiplex qPCR.

Results : Three ORF3 mutants were generated: an ORF3del mutant that contains a mutation in the start codon, a PSAP mutant that contains mutations in the C terminal late domain, and a CCC mutant that contains mutations in the N terminal cysteines 11-13 (a putative palmitoylation site). Replication and infectivity of all 3 mutants were comparable to the wild type (WT) HEV in vitro. WT ORF3 and the PSAP mutant predominantly localized to the apical membrane of HepG2 cells, whereas the CCC mutant was predominantly cytoplasmic. At sacrifice, HEV RNA was detectable in liver of 9/14 animals (1 animal died at 4 weeks pi), with HEV RNA titers (4-7 log IU/gr tissue) comparable between WT ($n=4/4$), PSAP ($n=4/4$) and CCC ($n=1/2$) inoculated mice. None of the ORF3del mutants proved infectious in vivo ($n=4/4$). While all WT inoculated mice had detectable HEV RNA in bile (5-7 log IU/mL) and feces (3-6 log IU/gr), only 1/4 PSAP mutant inoculated mice showed quantifiable HEV RNA in bile and feces. The HEV CCC mutant was barely detectable in bile < 3.75 log IU/mL and negative in fecal samples ($n=3/3$). Despite this, serum titers between WT-HEV PSAP and HEV CCC mutant viruses were comparable.

Conclusions : Overall this corroborates the importance of ORF3 in HEV propagation in vivo and suggests a role of a putative palmitoylation site at the N-terminus of ORF3 in secretion of HEV into the biliary canaliculi.

- A21 -

NON-INVASIVE SCREENING TEST IN PHYSIOLOGICAL CONDITIONS FOR PATIENTS WITH SUSPECTED BILIARY EXCRETION DISORDERS USING MRI WITH HEPATOSPECIFIC CONTRAST. C. Brussaard (1), J. Hendrickx (1), P. Gykiere (2), M. Vandewoude (3), J. de Mey (1) / [1] Universitair Ziekenhuis Brussel, Brussel, Belgium, Radiology, [2] Universitair Ziekenhuis Brussel, Brussel, Belgium, Nuclear Medicine, [3] Regionaal Ziekenhuis Tienen, Tienen, Belgium, Gastroenterology.

Introduction : There is a lack of reliable examinations for evaluation of biliary excretion time and testing sphincter of Oddi (SO) function. Dynamic ultrasound, dynamic T2 MRI sequences, and cholecystoscintigraphy are all performed under forced secretion (FS) and show variable sensitivity.

Aim : We describe a non-invasive MRI screening method with hepatospecific contrast (HSC) testing the SO in physiologic conditions.

Methods : Retrospective study: 35 consecutive pts (mean age 58.3 yrs, range 29-82 yrs, 8 men/27 women) underwent a standard MRI examination of the liver-biliary tree with HSC (Gd-EOB-DTPA) for characterizing a hepatic nodule. They had no complaints of SO dysfunction. The 3D T1 dynamic contrast series contained a series without contrast (t(0)) and a late phase at a variable time due to the dedicated protocol in function of the clinical question. Two radiologists judged in consensus whether the liver parenchyma and biliary tree are opacified and whether the contrast reaches the duodenum clearly in the late phase. Since scintigraphy with FS excludes SOD when the time between the start (t0) and the noticed activity in the duodenum (t(late phase)) is observed within 30 min, this was also our cut-off value.

Results : In all pts, the liver parenchyma and the biliary tree are opacified. Group A (19/35, 54%) shows clearly HSC in the duodenum in the late phase (t(0)-t(late phase) 25 ± 10 min). No excretion in the duodenum is noted in group B (16/35, t(0)-t(late phase) 19 ± 9 min). No significant differences between group A/B are noted for t(0)-t(late phase), age nor sex. In 15 pts, t(0)-t(late phase) is between 20-30 min. 11/15 (73%) pts belong to group A. 9/16 pts in group B and 5/19 pts in group A had a t(late phase) <20 min.

Conclusions : The liver enhances after IV administration of the HSC in the early vascular phase. However, the liver and the urinary excretory system are equally responsible (50%/50%) for the elimination of Gd-EOB-DTPA. So, the liver parenchyma enhances a second time in a later phase as the liver metabolizes it with subsequent excretion in the biliary tree and passing the SO in the duodenum. The product is metabolized in the same way as the metabolite in scintigraphy. In our population, 73% of the patients who had their final MRI sequence in the time frame between 20-30 min, showed the contrast in the duodenum, indicative for a normal biliary excretion time. This non-invasive MRI test is 100% specific. However, sensitivity is variable as no cut-off time in physiologic conditions is recommended. False negative results in our study are to be expected in group B with t(late phase) < 20 min (9/16 pts). This MRI test looks promising as a non-invasive screening tool for evaluation of disorders of biliary excretion (SO dysfunction, papillary stenosis/fibrosis, ...).

- A22 -

LARGE-SCALE SCREENING IS NOT USEFUL TO IDENTIFY INDIVIDUALS WITH HEPATITIS B OR C VIRUS INFECTION: FINAL RESULTS OF A SWISS PROSPECTIVE STUDY. A. Marot (1), A. Trabelsi (2), C. André (3), P. Deltenre (4) / [1] CHU UCL Namur, Yvoir, Belgium, Gastroenterology and Hepatology, [2] Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland, Gastroenterology and Hepatology, [3] Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland, Immunology and allergology, [4] Clinique Saint-luc Bouge, Namur, Belgium, Department of Gastroenterology and Hepatology.

Introduction : Current treatments are able to control HBV replication and to eradicate HCV in almost all cases. Further improvements in the management of HBV and HCV infections will be possible by focusing on treatment impact at a population level for which screening is an essential step. As many patients with HBV or HCV infection are still undiagnosed, large-scale screening could be useful.

Aim : To investigate whether large-scale screening for HBV or HCV infection (e.g. risk-based vs. age-based) could identify infected individuals.

Methods : Individuals between 18 and 80 years attending the pre-operative consultation prior to minor surgery in a general surgical outpatient clinic were tested for HBsAg, anti-HBc and anti-HCV from November 2014 to November 2018. The presence of anti-HCV was confirmed by an Immunodot test. HBV DNA and HCV RNA were determined in HBsAg- and anti-HCV-positive individuals.

Results : Among 3000 individuals tested, 7 were positive for HBsAg (0.26%) and 4 had detectable HBV DNA. Twelve individuals were positive for anti-HCV antibodies (0.44%). Two of them had detectable HCV RNA (0.07%) and 10 had

undetectable HCV RNA (5 spontaneously and 5 after a successful antiviral treatment). When compared to HCV negative people, HCV positive individuals had already been screened more frequently for HCV (83.3% vs. 12.8%, $p<0.001$) as well as for HBV infection (66.7% vs. 21.5%, $p=0.001$), had more frequently anti-HBc antibodies (33.3% vs. 4.2%, $p=0.001$), had more frequently HCV household members (16.7% vs. 1.7%, $p=0.02$), and had used more frequently intravenous drugs (66.7% vs. 0.1%, $p<0.001$), nasal drugs (58.3 vs. 6.2%, $p<0.001$) or cannabis (58.3% vs. 7.9%, $p<0.001$). None of HCV positive individuals were immigrant from an endemic area. The median age of HCV positive individuals was not different from that of those who were HCV-negative (52 years [range: 39-59] vs. 44 years [95% CI: 43-45], $p=0.1$). Most of the positive individuals were already aware that they were infected (86% of the HBV positive individuals and 100% of the HCV viremic individuals).

Conclusions : In this prospective study performed in a general surgical outpatient clinic, a large-scale screening was not useful to identify individuals with undiagnosed HBV or HCV infection. Screening for HBV and HCV infection should focus on individuals with well-known risk factors.

- A23 -

PATIENTS WITH CHRONIC HEPATITIS C VIRUS INFECTION ARE AT HIGH RISK OF BEING LOST TO FOLLOW UP. FOCUSED INTERVENTIONS CAN INCREASE LINKAGE TO CARE. H. Keymeulen (1), H. Van de Velde (1), A. Geerts (1), H. Van Vlierberghe (1), X. Verhelst (2) / [1] Ghent University Hospital, Ghent, Belgium, Gastroenterology and Hepatology, [2] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology and Hepatology.

Introduction : The main challenge in hepatitis C virus (HCV) treatment today is the identification of undiagnosed and untreated patients. A neglected group are patients once diagnosed with HCV virus infection who did not achieve viral eradication in the interferon era and were lost to follow-up.

Aim : The first goal of this work was to study the prevalence of patients who become lost to follow-up before HCV eradication was achieved and to identify risk factors associated with this phenomenon. The second goal was to reach out to patients lost-to-follow up in order to identify risk factors for this behaviour and try to restore linkage to care.

Methods : First, a cross-sectional study was performed in a tertiary liver unit. All patients who ever visited the outpatient clinic for HCV infection between 2000 and 2017 were eligible. Demographic and clinical data were retrieved from the electronic patient files. We focused on successful eradication and occurrence of lost-to-follow up. Risk factors for lost-to-follow up were searched for using univariate and multivariate analysis. Second, patients lost-to follow up were contacted by phone in order to inquire about their further HCV-related medical history using a standardised flowchart. Patients were questioned about their current infection status, previous treatment and risk factors for getting lost-to-follow up.

Results : In this study, 427 patients could be identified with HCV infection. Ninetythree patients (21.8%) were lost to follow-up. Patients who inject drugs (PWID) and patients who received no treatment had a higher risk to become lost to follow-up (OR=2.225; $p=0.003$; 95% CI:1.319-3.854 and OR=2.177; $p=0.016$; 95% CI:1.153-3.894, respectively). In contrast, patients who received two or more treatment lines showed a lower risk (OR=0.215; $p<0.001$; 95% CI: 0.094-0.491). Of the 93 lost to follow-up patients, only 34 patients (36.6%) could be reached. Ten patients (10.8%) were treated in another hospital. The other 24 patients (25.8%) were not in follow-up and did not receive treatment. The main reason to interrupt follow-up and refuse treatment was anxiety for side effects of the therapy in the interferon era. Nine patients (9.7%) were interested in obtaining more information about the new treatment with DAAs. Eight patients (8.6%) were already cured during their follow-up in our center, in the gap between data acquisition and analysis. Fifty-nine patients (63.4%) were unreachable. Of these, 18 patients (19.4%) were deceased, 27 patients (29.0%) had no contact details and 14 patients (15.1%) never answered the phone.

Conclusions : Patients with chronic HCV infection had a high risk to get lost to follow up in the pre-DAA era. Main risk factors are PWID and being untreated after a first medical contact. Focused patients recall actions by phoning patients or the primary physician can increase linkage to care and results in more patients being treated for HCV infection.

- A24 -

TESTING FOR VIRAL HEPATITIS B AND C BY GENERAL PRACTITIONERS IN FLANDERS, BELGIUM. R. Bielen (1), Ö. Koc (1), D. Busschots (1), G. Robaey (2), B. Aertgeerts (3), B. Vaes (3), P. Mamouris (4), C. Matheï (3), G. Goderis (5), F. Nevens (6) / [1] Hasselt University, Hasselt, Belgium, Faculty of Medicine and Life Sciences, [2] Ziekenhuis Oost Limburg (ZOL), Genk, Belgium, Gastroenterology, [3] Katholieke Universiteit Leuven, Leuven, Belgium, Public Health and Primary Care, [4] Katholieke Universiteit Leuven, Leuven, Belgium, Public Health and Primary Care, [5] Katholieke Universiteit Leuven, Leuven, Belgium, Public Health and Primary Care, [6] University Hospitals Leuven, Leuven, Belgium, Gastroenterology and Hepatology.

Introduction : Chronic infections with hepatitis B virus (HBV) and hepatitis C virus (HCV) have a major impact on mortality worldwide. Although effective treatments are available for both HBV and HCV infection, less than 50% of

the patients are even diagnosed in Belgium. This study assessed the real-life testing – and diagnosis rate by general practitioners (GPs) in Flanders, Belgium.

Aim : To assess the testing rate for HBV and HCV infection in 48 primary care practices in the INTEGO project in Flanders, Belgium.

Methods : INTEGO contains data of 440,140 patients over 20 years, which corresponds to 2.2% of the total Flemish population yearly. The primary care practices are distributed across Flanders and the INTEGO patient population is representative for the distribution of age, gender, and socio-economic status at the community level.

Results : Of 440,140 patients included in INTEGO, 7,892 (1.8%) patients were screened for hepatitis B surface antigen (HBsAg) and 7,206 (1.6%) for HCV antibody (Ab) of whom 369 (4.7%) and 163 (2.3%) tested positive, respectively. Of 14,059 patients with chronic liver enzyme elevation, 1,112 (7.9%) and 1,395 (9.9%) were tested for HBsAg and HCV Ab.

Conclusions : This study demonstrates that real-life testing uptake for viral hepatitis B and C is suboptimal in the general practices in Flanders, even in patients with chronically elevated liver enzymes. As GPs play a crucial role in prevention, diagnosis and linkage to care, efforts and strategies to increase the testing uptake for HBV and HCV are urgently needed.

- A25 -

HEPATITIS C NURSE AS A CASE MANAGER IN PEOPLE WHO INJECT DRUGS. R. Bielen (1), E. Dercon (2), Ö. Koc (1), D. Busschots (1), L. Vinken (2), R. Verrando (2), K. Vanhees (3), F. Nevens (4), G. Robaey (5) / [1] Hasselt University, Hasselt, Belgium, Faculty of Medicine and Life Sciences, [2] Center for Alcohol and other Drugs (CAD) Limburg, Belgium, MSOC, [3] University Biobank Limburg (UBiLim), Belgium, Biobank, [4] University Hospitals Leuven, Leuven, Belgium, Gastroenterology and Hepatology, [5] Ziekenhuis Oost Limburg (ZOL), Genk, Belgium, Gastroenterology.

Introduction : Despite the high hepatitis C virus (HCV) prevalence in people who inject drugs (PWID), the uptake for HCV care is low in Belgium. In Limburg, this uptake was increased by case management performed by a medical doctor in 2015. We studied whether an increase in uptake of HCV care could also be achieved with a HCV nurse as a case manager.

Aim : To study the effect of case management by a HCV nurse on the screening uptake, linkage to care and treatment uptake of people who inject drugs for HCV infection.

Methods : In this ongoing prospective cohort study, which started in November 2016, case management is performed by a HCV nurse. The nurse informs PWID about HCV, and performs screening (anti-HCV with reflex HCV-RNA) on-site by venepuncture. All HCV RNA positive PWID are referred to the hospital by the nurse, who accompanies them if necessary. After successful cure, information on prevention of reinfection is provided with yearly follow-up of HCV RNA status. Intermediate results were compared to the pilot project performed by a medical doctor in the same setting in 2015.

Results : In 2015 and 2017, 310 and 321 clients received opiate agonist therapy in Limburg, respectively. The case manager personally informed 236/310 (76.1%) and 246/321 (76.6%), $p=.925$. Out of the 236 and 246 informed clients, 198 (83.8%) and 194 (78.8%) accepted on-site screening, $p=.412$. Linkage to care was high in the HCV RNA positive PWID: 42/56 (75.0%) in 2015 and 43/58 (74.1%) in 2017, $p=.916$. Eligibility for treatment was 34/42 (80.9%) and 39/43 (90.6%), $p=.197$. Nevertheless, uptake for treatment was low due to stringent reimbursement criteria in Belgium (>F3 in 2015, >F2 in 2017) and only 15/56 (26.8%) patients could be started in 2015 vs. 18/58 (31.0%) in 2017, $p=.685$. One reinfection was diagnosed (different genotype) 25 months after reaching end-of-treatment response.

Conclusions : Case management can be performed equally well by a HCV nurse as by a medical doctor. Rates of uptake for screening and linkage to care are high. This approach helps to identify the remaining gaps, and improvements like point-of-care testing and outreach will be implemented next year.

- A26 -

UPTAKE OF TREATMENT FOR HEPATITIS C INFECTION IN PEOPLE WHO INJECT DRUGS: THE LINK STUDY. R. Bielen (1), A. Arain (1), D. Busschots (1), Ö. Koc (1), F. Nevens (2), C. Trabert (3), J. Werenne (4), N. Leonardy (5), J. Mulkay (6), S. Bourgeois (7), C. Matheï (8), G. Robaey (9) / [1] Hasselt University, Hasselt, Belgium, Faculty of Medicine and Life Sciences, [2] University Hospitals Leuven, Leuven, Belgium, Gastroenterology and Hepatology, [3] C.A.P. Fly asbl Liège, Belgium, MSOC, [4] Projet LAMA asbl Bruxelles, Belgium, MSOC, [5] Maison d'Accueil Socio-Sanitaire (MASS) asbl Bruxelles, Belgium, MSOC, [6] Hôpital Saint-Pierre Bruxelles, Belgium, Gastroenterology and Hepatology, [7] ZNA Antwerpen, Antwerpen, Belgium, Gastroenterology and Hepatology, [8] Free Clinic vzw Antwerp, Belgium, MSOC, [9] Ziekenhuis Oost Limburg (ZOL), Genk, Belgium, Gastroenterology.

Introduction : Treating people who inject drugs (PWID) for a chronic hepatitis C viral (HCV) infection is a necessity in order to reach the 2030 targets of the World Health Organization. Nevertheless, treatment uptake is low in PWID.

Aim : To study the factors influencing treatment uptake in PWID in Belgium.

Methods : We performed a prospective, multi-center observational study. Between June 2012 and November 2016, clients were enrolled in 7 opiate agonist treatment (OAT) centres in Belgium. A questionnaire was performed at inclusion, after one and two years. Follow-up was ceased after two years, or earlier if a client was treated for HCV infection. Factors influencing treatment uptake ($p < 0.10$) upon univariate analysis were analyzed in a logistic regression model with backward conditional removal of insignificant factors ($p \geq 0.05$).

Results : Of 255 enrolled clients, 71 (27.8%) were treated for HCV infection within the two year follow-up period. In our final model, clients were more likely to be treated based on the participating OAT centre (OR 12.00(1.76 -81.68)), gender (being male: OR 4.74 (1.29-17.36)), based on netto income (>700 euro/month: OR 5.47 (1.36-21.95)), treatment willingness (OR 13.77 (1.34-141.34)), investigation by liver biopsy or fibroscan allready performed (OR 11.21 (4.56-27.60) and 3.94 (1.51-10.27) respectively), and if they were referred by the center to a hospital (OR 2.96 (0.99-8.88)).

Conclusions : Treatment uptake was low in this well-defined group of PWID on OAT. Differences in treatment uptake were due to factors influenced by linkage to care (treatment willingness, further investigation and referral) and less by social factors (active drug use, social functioning). To increase the uptake of treatment, actions influencing linkage to care should be undertaken

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FIRST LINE SCREENING BY FIBROSCAN (TRANSIANT ELASTOGRAPHY) IN A POPULATION AT HIGH RISK FOR HCV INFECTION. F. Desselle (1) / [1] CHC, Liège, Belgium, Gastro-enterology.

Introduction : Patients who inject drugs (PWID) are at high risk for HCV infection. Unfortunately, they usually do not receive adequate care although they should be considered top-priority for HCV treatment considering the elevated risk of transmission. Furthermore, most of them are not aware of their HCV infection. Currently, Belgian patients can only access treatment if they show a significant fibrosis (Metavir \geq F2).

Aim : The aim of this study is to assess the efficacy of Fibroscan as screening procedure in first line care centers to improve PWID management.

Methods : For 1 year, PWID from 3 first line care centers in Liège, Belgium, were offered Fibroscan. Those with unknown HCV status were also offered an HCV screening by Rapid Diagnostic Test (RDT).

Results : 92 Fibroscans were performed (acceptation rate of 60,3%). 55 patients (59,8%) reported HCV positivity prior to the study, 15 (16,3%) had a negative serological status. 22 patients (23,9%) had undetermined serological status prior to the study and 21 of them underwent a RDT. RDT was positive for 11 patients; 2 PCR were performed and were positive. 80,4% of the Fibroscans were reliable. 29 patients (32,6%) had significant fibrosis (Metavir \geq F2); among them 13 (44.8%) agreed to attend an outpatient hepatology clinic; 10 were HCV positive and 3 were HCV negative. HCV treatment could be initiated in 5 out of the 10 HCV positive patients.

Conclusions : Fibroscan is a useful, non-expensive, easy to handle, noninvasive tool to screen PWID for liver fibrosis. Fibroscan combined with RDT should help to convince this reluctant population to accept adequate medical care and to refer HCV patients who are eligible for treatment to an outpatient hepatology clinic. It is also helpful to refer patients with liver fibrosis due to other etiologies and globally improve PWID management.

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MYELOID-SPECIFIC IRE1 ALPHA DELETION REDUCES TUMOUR DEVELOPMENT IN A NON-ALCOHOLIC STEATOHEPATITIS-INDUCED HEPATOCELLULAR CARCINOMA MOUSE MODEL. S. Van Campenhout (1), S. Lefere (1), A. Vandierendonck (1), A. Geerts (1), X. Verhelst (1), H. Van Vlierberghe (1), L. Devisscher (2) / [1] Ghent University, Ghent, Belgium, Internal Medicine and Pediatrics, [2] Ghent University, Ghent, Belgium, Basic and Applied Medical Sciences.

Introduction : Obesity, diabetes and associated non-alcoholic steatohepatitis (NASH) are characterized by adipose tissue and hepatic fat accumulation and inflammation and are rising causes of hepatocellular carcinoma (HCC). Macrophages are important immune cells involved in inflammation and tumour development. Macrophage inositol-requiring enzyme 1 alpha (IRE1a), an ER-stress protein, has shown to be involved in macrophage cytokine production and myeloid-specific IRE1a knock-out (KO) mice showed reduced weight gain during high fat diet feeding. However, the effect on NASH and subsequent HCC development has not been examined.

Aim : We investigated the effect of myeloid-specific IRE1a deletion on experimental NASH-HCC development.

Methods : Mice with non-functional myeloid IRE1a were created by crossing IRE1a floxed mice with LysM-Cre mice. Two-day old KO and wild type (WT) mice were subcutaneously injected with streptozotocin (STZ) and male mice were fed a high-fat, -sucrose, -cholesterol diet (shortly called HFD) from the age of 4 weeks till 21 weeks. Control KO and WT mice received a PBS injection and matched control diet. Mice were evaluated for obesity, diabetes, NASH and HCC by analyses of serum, fat and liver samples.

Results : STZ injection resulted in lower body weights at the age of 4 weeks (start of HFD) compared to control mice and resulted in elevated fasting glucose levels in STZ-WT mice, which was not observed in STZ-KO mice. HFD feeding resulted in more fat accumulation ($p = 0.009$) and a higher body weight ($p = 0.05$) but attenuated glucose intolerance ($p = 0.01$ at peak glucose levels) in STZ-KO mice compared to STZ-WT mice. While no difference was observed in the NAFLD activity score between STZ-KO and STZ-WT mice after HFD feeding, STZ-KO mice presented with significant lower tumour loads ($p = 0.009$) and reduced alpha fetoprotein gene expression both in tumour and surrounding tissue compared to STZ-WT mice. Liver monocyte infiltration was significantly higher ($p = 0.01$) and pro-inflammatory cytokine induction tended to be more pronounced in STZ-KO mice compared to STZ-WT mice after HFD feeding whereas the control KO mice showed a tendency to lower levels of pro-inflammatory markers and liver monocytes compared to control WT mice under homeostatic conditions.

Conclusions : Our results indicate that myeloid-specific IRE1a deletion attenuates diabetes induction and results in reduced NASH-induced HCC without significant influence on HFD-induced NASH development.

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ELIMINATING VIRAL HEPATITIS C IN BELGIUM: A MATHEMATICAL MODEL OF THE MICRO-ELIMINATION APPROACH. D. Busschots (1), S. Toghanian (2), R. Bielen (1), S. Salomonsson (2), Ö. Koc (1), G. Hendrickx (3), M. Jadoul (4), F. Nevens (5), E. Sokal (6), C. Brixko (7), K. Peerlinck (8), L. Apers (9), G. Robaeys (10), J. Lazarus (11) / [1] Hasselt University, Hasselt, Belgium, Faculty of Medicine and Life Sciences, [2] MSD Sweden, Stockholm, Sweden, Center of Observational Real-World Evidence (CORE), [3] University of Antwerp, Antwerp, Belgium, Viral Hepatitis Prevention Board, Centre for the Evaluation of Vaccination, Vaccine & Infectious Diseases Institute, [4] Université Catholique de Louvain, Brussels, Belgium, Service de Néphrologie, Cliniques Universitaires Saint-Luc, [5] University Hospitals Leuven, Belgium, Departement of Gastroenterology and Hepatology, [6] Université Catholique de Louvain, Brussels, Belgium, Service Gastroentérologie Hépatologie Pédiatrique, Cliniques Universitaires Saint-Luc, [7] CHR Citadelle, Liège, Belgium, Department of Gastroenterology and Digestive Oncology, [8] University Hospitals Leuven, , Belgium, Division of Cardiovascular Disorders, Haemophilia Center, [9] Institute of Tropical Medicine Antwerp, Antwerp, Belgium, Department of Clinical Sciences, [10] Ziekenhuis Oost Limburg (ZOL), Genk, Belgium, Department of Gastroenterology and Hepatology, [11] University of Barcelona, Barcelona, Spain, Barcelona Institute for Global Health (ISGlobal), Hospital Clinic.

Introduction : The hepatitis C virus is one of the leading causes of chronic liver disease and liver-related deaths worldwide, prompting the World Health Organization to define targets for eliminating it by 2030. Belgium has had a ‘Hepatitis C Plan’ since 2014, yet elimination efforts remain unclear. The estimated prevalence is low in the general population (0.57%), though higher in several subgroups.

Aim : This study sets out to employ the best available data to construct a micro-elimination model to guide national efforts.

Methods : A constrained optimization modelling approach was applied for developing the “HepC Countdown” model in Excel with the objective to demonstrate how many patients need to be treated to reach elimination of hepatitis C by 2030, based on reported or estimated prevalence, incidence and reinfection rates (just for PWID) and current versus alternative treatment rates. Six subgroups with increased risk of hepatitis C were studied: people living with HIV, haemodialysis patients, migrants, patients with advanced liver disease, people who inject drugs and prisoners.

Results : According to the model, none of the subgroups would achieve hepatitis C elimination by 2030 at current treatment rates (Table 1). With the current rate of 3%, hepatitis C elimination would be reached by 2057 at the earliest in all subgroups with the exception of PWID (2314). For Belgium to meet the WHO targets, the average percentage of patients to treat per year out of the total pool of patients to be treated needs to be fixed at 8% of the current patient pool.

Conclusions : In order to reach the WHO elimination targets much greater efforts are required in Belgium, including removing hepatitis C treatment reimbursement restrictions. Improving surveillance and prevention would further facilitate efforts.

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FIRST BELGIAN HEPATITIS E SEROPREVALENCE STUDY SHOWS LOW STABLE BIRTH-COHORT SPECIFIC SEROPREVALENCE UNTIL 2014, WITH RECENT 2016-2018 INCREASE IN SINGLE CENTRE ESTIMATES. E. Ho (1), V. Hutse (2), V. Verburch (2), M. Jacques (2), H. Theeten (3), A. Lizroth (4), V. Suin (2), S. Van Gucht (2), S. Blaizot (3), A. Rahman (3), N. Hens (3), P. Van Damme (3), P. Michielsens (5), T. Vanwolleghem (5) / [1] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology and Hepatology, [2] Sciensano, Brussels, Belgium, Viral Diseases, [3] University of Antwerp, Antwerp, Belgium, Vaccine and Infectious Diseases Institute, [4] Sciensano, Brussels, Belgium, Epidemiology of infectious diseases, [5] Universiteit Antwerpen / Antwerp University Hospital, WILRIJK (Antwerpen), Belgium, Gastroenterology and Hepatology.

Introduction : Recent studies have shown rising seroprevalence of hepatitis E virus (HEV) in younger age cohorts in Europe, but substantial regional differences are found.

Aim : We aimed to evaluate trends in time in birth cohort-specific HEV seroprevalence and regional differences in Belgium.

Methods : Firstly, we performed a retrospective analysis of HEV IgG seroprevalence on two national serum banks obtained from sentinel laboratories in 2006 and 2014. Five to ten-year age cohorts held equal amounts of samples and were equally distributed in sex and regional origin. Secondly, a prospective, single centre HEV IgG evaluation was performed of 1200 patients visiting the Hepatology department between 2016 and 2018. Wantai anti-HEV IgG ELISA assays were performed. Results equal or above 1.1 OD/cutoff were considered positive, below 1.1 as negative. Statistical analysis with R included a one-sided power analysis to specifically estimate required sampling for birth cohort-specific seroprevalence evaluation (1604 and 2087 samples respectively). Chi-square analysis or Fisher's Exact Test was performed in SPSS 25 to compare sex, region and birth cohort proportions.

Results : Overall HEV IgG seroprevalences were 4.7% (76/1604, CI 3.2-6.3) and 5.8% (121/2087, CI 4.5-7.1) in 2006 and 2014 ($p=0.161$), respectively. In the single centre analysis, HEV IgG seroprevalences were 8.6% (43/499, CI 6.2-11.1) and 17.1% (120/701, CI 14.3-19.9) in 2016 and 2018 ($p < 0.001$), respectively. No significant differences between sexes were found for any of the years ($p=0.603$, $p=0.942$, $p=0.944$, $p=0.657$). Significant regional differences were found in 2014 ($p=0.021$) with a significant rise between 2006 and 2014 in two provinces: Hainaut (1.5% to 6.0%, $p=0.043$) and Namur (3.7% to 14.7%, $p=0.037$). We found no significant birth cohort-specific differences between 2006 and 2014, but in the single centre analysis we found a significant increase between 2016 and 2018 in the two oldest birth cohorts (born 1942-1947: 11.9% to 27.3%, $p=0.028$ and born 1948-1953: 15.4% to 41%, $p=0.002$).

Conclusions : Compared to reported seroprevalences in surrounding countries, initial analysis of Belgian nationwide HEV IgG seroprevalence shows stable and rather low rates. No birth cohort-specific increase in seroprevalence is seen between 2006 and 2014. A regional increase of seroprevalence was however found in two south-western provinces. In addition, single centre analysis between 2016 and 2018 suggests a recent rising seroprevalence, especially in older birth cohorts.

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THE PREVALENCE AND RISK FACTORS OF HEPATITIS B VIRAL INFECTION IN MIDDLE LIMBURG BELGIUM: THE IMPORTANCE OF MIGRATION. Ö. Koc (1), C. Kremer (2), R. Bielen (1), D. Busschots (1), N. Hens (2), F. Nevens (3), G. Robaey (4) / [1] Hasselt University, Hasselt, Belgium, Faculty of Medicine and Life Sciences, [2] Hasselt University, Hasselt, Belgium, Interuniversity Institute for Biostatistics and statistical Bioinformatics (I-Biostat), [3] KU Leuven, Belgium, Gastroenterology and Hepatology, [4] Ziekenhuis Oost Limburg (ZOL), Genk, Belgium, Gastro-enterology and Hepatology.

Introduction : The hepatitis B virus (HBV) prevalence study performed in Flanders Belgium in 2003 is believed to be an underestimation due to underrepresentation of the non-Belgian population.

Aim : Due to the lack of other data, the present study re-evaluated the current prevalence and risk factors of HBV infection in a multi-ethnic region situated in Middle-Limburg, Belgium.

Methods : Between May and November 2017, patients aged 18-70 years who presented at the emergency department of a large teaching hospital in Middle-Limburg, were invited to participate in this study. Upon informed consent, a questionnaire was performed assessing demographics, viral hepatitis status and risk factors. Blood samples were tested for hepatitis B surface antigen and antibodies against hepatitis B core antigen (anti-HBc).

Results : Of the 1,537 patients invited, 1,131 (73.59%) participated in the study. First-generation migrants (FGMs) comprised 20.78% of the study population and were mainly born in the Netherlands (32.77%), Turkey (18.72%), and Italy (12.34%). The overall prevalence of chronic HBV infection was 0.97%, with differences between Belgians (0.56%) and first-generation-migrants (2.55%), ($p = .016$). Out of 11 chronically HBV infected individuals, five (45.5%) were not aware of their HBV status and the other six (54.5%) were already linked to care. All five (100%) newly diagnosed chronic HBV patients had further clinical evaluation and all had a normal level of alanine-aminotransferase. The prevalence of hepatitis B core antibodies was 8.4%, and was significantly associated with age-gender-ethnicity interaction, presence of HBV infected household member, hepatitis C virus infection, men who have sex with men, and haemodialysis.

Conclusions : In this area with large immigrant populations, we found a higher prevalence of chronic HBV infection compared to the nationwide study of 2003. National HBV screening for first-generation migrants is needed as this high-risk group will go unnoticed due to the possible incorrect interpretation of normal alanine-aminotransferase values.

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COMPUTED TOMOGRAPHY ASSISTED MEASUREMENT OF VISCERAL ADIPOSE TISSUE VOLUME AND SUBCUTANEOUS ADIPOSE TISSUE VOLUME CAN DIFFERENTIATE BETWEEN SIMPLE STEATOSIS AND

NON-ALCOHOLIC STEATOHEPATITIS. J. Dierickx (1), C. Lecluyse (1), P. Smeets (1), S. Lefere (2), B. Lapauw (3), H. Van Vlierberghe (2), A. Geerts (2), X. Verhelst (2) / [1] UZ Gent, Gent, Belgium, Radiology, [2] UZ Gent, Gent, Belgium, Gastroenterology, [3] UZ Gent, Gent, Belgium, Endocrinology.

Introduction : Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease and is associated with the metabolic syndrome. Current non-invasive procedures, like elastography, CT scan of the liver and biochemical tests cannot differentiate simple steatosis from non-alcoholic steatohepatitis (NASH). Liver biopsy is still the golden standard to diagnose NASH.

Aim : To investigate the correlation between visceral, subcutaneous, deep subcutaneous and superficial subcutaneous adipose tissue and NASH.

Methods : 32 patients, who visited the Ghent University Hospital between 2005 and 2017, were retrospectively included in this study. Results of liver biopsy specimens were retrospectively collected. CT scans were re-analysed and visceral adipose tissue volume (VATV; cm³), subcutaneous adipose tissue volume (SATV; cm³), deep subcutaneous adipose tissue volume (dSATV; cm³) and superficial subcutaneous adipose tissue (sSATV; cm³) were measured, using syngo. via software, and corrected by BMI and total adipose tissue volume (TATV). SPSS statistics was used for univariate analysis.

Results : VATV (p=0,035) and VATV/BMI index (p=0,007) correlated significantly with NASH. The area under the curve (AUC) of the VATV/BMI index is 0,811. The cut-off point 1,6674 cm³ m² kg⁻¹ has a sensitivity of 94,44%, a specificity of 60,00%, a positive predictive value of 80,95% and a negative predictive value of 85,71%. NASH patients have a significantly lower sSATV (p=0,027), sSATV/BMI index (p=0,034), sSATV/TATV index (p=0,005) and SATV/TATV index (p=0,042). dSATV could not be correlated to NASH.

Conclusions : The VATV, corrected by total adipose tissue, can be used as a biomarker to exclude NASH. sSATV, corrected by total adipose tissue, and SATV/TATV are inversely correlated with NASH. CT scan quantifies the abdominal adipose tissue distribution and can be considered as a non-invasive tool to differentiate hepatic steatosis and NASH.

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PREVALENCE AND SCREENING OF HEPATITIS C IN BELGIUM IN 2015-2017. L. Lasser (1), P. Stärkel (2), C. Moreno (3), B. Deressa (4), O. Elkilic (4), M. Ngassa (4), E. De Koster (4) / [1] CHU Brugmann, Brussels, Belgium, gastroentérologie, [2] Clin universitaires St-Luc, UCL, Brussels, Belgium, Hepatogastroenterology, [3] Hopital Erasme, ULB, Belgium, Hepatogastroenterology, [4] CHU Brugmann, Brussels, Belgium, Hepatogastroenterology.

Introduction : Recent analyses in hepatitis C (HCV) have shown that increasing efficacy of treatment with direct acting antiviral agents (DAA) alone will not be able to reduce the HCV disease burden. Higher efficacy therapies should be combined with increased diagnosis and treatment rate. Recently birth cohort screening recommendations were developed in the United States. In Belgium no recent prevalence studies have been conducted. The most cited anti-HCV prevalence is 0.87% based on a study in the Flemish population published in 1997 but collected in 1994. The diagnosis rate of HCV in Belgium is estimated at 43%, signifying that more than 50% of HCV patients remain undiagnosed. Moreover no formal screening strategy exists in Belgium. A birth cohort analysis based on a model suggests a birth cohort between 1950 and 1975 in Belgium. This population should reflect 70% of the viremic population.

Aim : The goal of this study was to estimate the prevalence of hepatitis C in Belgium in 2015-2017 and to confirm the proposed targeted birth cohort and other risk factors.

Methods : Between 01/09/2015 and 31/12/2017 patients coming to the laboratory for a blood sample or admitted to the one day clinic for surgery and gastroenterology were asked, after signing an informed consent, to perform an HCV serology. On a voluntary basis patients could fill in a questionnaire about HCV risk factors. In case of a positive serology test, the patients were contacted and proposed to realize a classic work up and discuss therapeutic options, if necessary.

Results : A total of 1975 patients (1200 women /975 men) were included of whom 1897 performed an HCV serology. The mean age of the screened population was 49.89 years. The majority of patients were Caucasian (71%). 12% patients were Northern-African, 7% were Black-African and 4% were from the Middle East. 22 patients (12 women / 10 men) had a positive serology, realising a prevalence of 1.16%. The mean age of the seropositive population was 61.5 years. Most of them were Caucasian (9 patients) or African (9 Black-African and 2 Northern African). The major risk factor was medical care and/or dialysis in the country of origin. A PCR was done in 17 of the 22 patients and 5 of them had a positive viral load. Four patients with negative PCR were previously treated in the past with success. Genotype data were available in 8 patients (1 genotype 1a, 1 genotype 1b, 1 genotype 2, 1 genotype 3 and 4 genotype 4). Only three patients were newly diagnosed. Concerning the distribution of patients in relation to the different birth cohorts, the highest prevalence of 1.6% was found in the cohort between 1940 and 1965 (14/858) followed by the cohort between 1945 and 1970 with a prevalence of 1.4% (14/986). The suggested birth cohort between 1950-1975 showed a lower prevalence of 1.2% (12/975).

Conclusions : In our study we found a higher seroprevalence of 1.16% compared to the previously assumed prevalence of 0.87%. This can be due to the fact that the study was done in an higher at risk urban population not really representative

for the all Belgian population. Furthermore our study could not confirm the suggested birth cohort (1950-1975). Our data evoke another birth cohort of 1940-1965. Finally this screening strategy was not effective in detecting new patients because only three new patients were diagnosed. Larger studies or pooled data from other realised screening studies are certainly warranted. These data could than provide an efficient source of identifying newly diagnosed patients as part of a national screening strategy.

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C60 FULLERENE INHIBITS FIBROSIS AND INITIAL STAGES OF LIVER CARCINOGENESIS ON RAT MODEL OF DEN+CCL4-INDUCED HEPATOCELLULAR CARCINOMA. H. Kuznietsova (1), N. Dziubenko (1), T. Herheliuk (2), O. Perepelytsina (2), Y. Prylutsyy (1), U. Ritter (3), P. Scharff (3), V. Rybalchenko (1) / [1] Taras Shevchenko National University, Kyiv, Ukraine, Institute of Biology and Medicine, [2] Institute for Problems of Cryobiology and Cryomedicine, 61015, Ukraine, Department of Biotechnical Problems in Diagnostic, [3] Technische Universität Ilmenau, Ilmenau, Germany, Institute of Chemistry and Biotechnology.

Introduction : Hepatic cancer occupies one of the leading causes for deaths from cancer in the World. This pathology is poorly diagnosed, has an extremely unfavorable prognosis and lack of effective medication therapy. Hepatocellular carcinoma (HCC) accounts for 80-90% of all liver primary malignant tumors. HCC develops according to the scheme: progressive inflammation followed by fibrosis and cirrhosis, followed by malignant degeneration. The excessive production of reactive oxygen species is the main cause and trigger of all abovementioned processes, therefore the use of antioxidants could be considered as an appropriate treatment of those. Biocompatible water soluble C60 fullerenes have the powerful antioxidant properties, are non-toxic in in vitro and in vivo systems if acting in physiological concentrations and capable for accumulation in liver, so are attractive for direct impact on that.

Aim : The effects of C60 fullerenes on liver state under fibrosis and initial stage of carcinogenesis on rat HCC model and on EGFR and cytokeratin (CK) receptors expression in HepG2 cell line were aimed to be discovered.

Methods : Sixty male Wistar rats 5 weeks old were divided on 6 groups (n=10). HCC was initiated by single N-diethylnitrosamine (DEN, 200 mg/kg) intraperitoneal injection. Two weeks from DEN injection tumor promotion was achieved by subcutaneous injection of CCl₄ (0.1 ml/100g) twice/week continuously for 8 and 13 weeks. In 10 weeks after HCC initiation liver fibrosis develops, and 15th week corresponds to cell malignant transformation stage. Pristine C60 fullerene aqueous colloid solution (C60FAS; initial concentration 0.15 mg/ml) was administered daily intraperitoneally at dose of 0.25 mg/kg starting in 2 weeks from DEN injection. Liver injury was evaluated according to 13-point scale, α -amylase, ALT, AST, ALP, LDH, conjugated and unconjugated bilirubin, urea, creatinine and total protein were measured in blood serum. EGFR and CK receptors expression in HepG2 cells (human HCC) were assessed immunohistochemically after 48 h incubation with 10 and 100 μ g/ml C60FAS.

Results : Non-treated animals experienced HCC at 10-week stage demonstrated liver damage score 8.2 points (steatohepatosis and micronodular fibrosis). Although ALT, AST and bilirubin were unchanged compared to control, ALP and LDH increased by 1.6 and 3.2 times, respectively. Such changes (ALP and LDH growth under unchanged ALT, AST and bilirubin) may indicate intrahepatic cholestasis, biliary cirrhosis, and even liver cells neoplasia. C60FAS decreased liver injury to 7.25 points (micronodular fibrosis occurred but was less expressed) and normalized ALP and LDH. However, ALT and AST were elevated (by 4 and 3.7 times, respectively), as well as creatinine (by 35%) and urea (by 40%). This might indicate inhibition of liver fibrogenesis and neoplastic transformation but, at the same time, hepatocytes injury and renal insufficiency. Liver functional activity, however, corresponded to control (bilirubin was unchanged). In HCC 15-week stage liver injury progressed in all animals. Liver damage score in non-treated rats corresponded to 9.2 points (macronodular fibrosis and cirrhosis); in 6 out of 10 animals single tumor nodes (1 per animal) were detected; ALP and LDH dramatically increased (by 4.5 and 28.5 times, respectively); ALT, AST, conjugated and unconjugated bilirubin also tended up (by 2.9, 2.8, 2.3 and 1.7 times, respectively), suggesting cirrhosis, cell neoplastic transformation, hepatocytes destruction and hepatic insufficiency. C60FAS diminished liver injury to 7.8 points (micronodular fibrosis), depressed ALP and LDH (by 16% and 61% compared to HCC non-treated animals) and normalized bilirubin. However, ALT and AST remained increased, serum creatinine and urea also grew up by 24% and 87%, respectively. These findings allow us to suggest the inhibition of fibrogenesis and cell malignant transformation and normalization of liver functional activity. However, hepatocytes injury and renal insufficiency also occurred. C60FAS inhibited expression of EGFR and CK receptors in HepG2 cells in a dose-dependent manner by 70% and 63%, respectively, acting in maximum concentration.

Conclusions : Thus, the ability of C60FAS to inhibit the processes of fibrogenesis and malignant degeneration in liver and to maintain its functional activity was concluded. However, increased aminotransferases and renal dysfunction also occurred. These C60 effects could be realized through inhibition of EGFR and CK receptors expression in liver cells.

RELATIONSHIP BETWEEN INTESTINAL PERMEABILITY AND INFLAMMATION AND SEVERITY OF ALCOHOLIC LIVER DISEASE. L. Maccioni (1), B. Pirlet (1), I. Leclercq (1), P. Stärkel (2) / [1] Laboratory of Gastroenterology, Institut de Recherche Expérimentale et Clinique, Woluwe-Saint-Lambert, Belgium, Department of Hepato-Gastroenterology, [2] Cliniques Universitaires Saint-Luc, Brussels, Belgium, Department of Hepato-Gastroenterology.

Introduction : Heavy alcohol consumption is one of the leading causes of chronic liver disease and liver-related death worldwide. Although up to 90 % of alcoholics develop steatosis, only a minority of those with fatty liver progress to alcoholic steato-hepatitis and 10-20 % eventually develop cirrhosis. Recent data from animal models of ALD suggest the existence of a gut-liver axis playing an important role in the progression of the disease. Indeed, alcohol-induced disruption of the intestinal epithelial barrier, leading to increased gut permeability, also called “leaky gut”, qualitative changes in the composition of the gut microbiota, also known as “dysbiosis”, and translocation of bacterial products into the portal circulation could then potentially contribute to the progression of alcoholic liver disease. However, data in humans to sustain this mechanism are currently lacking.

Aim : This study aimed to assess in a well characterized cohort of alcohol dependent patients the connections between severity of liver disease, intestinal permeability and the inflammatory status of the small bowel mucosa, in order to give a better insight into the dialogue between these two organs in humans.

Methods : Alcohol-dependent patients admitted to the alcohol withdrawal unit were included in the study. All subjects kept drinking until the day of admission. Liver function tests (AST, ALT, GGT, ALP, bilirubin, INR, albumin) and Fibroscan® combined with the controlled attenuation parameter (CAP) were performed at the day of admission. Liver Doppler ultrasound and a gastroscopy with distal duodenal biopsies were obtained on the following day. Based on these parameters, patients were then classified according to their liver features as follows: Subjects with no signs of liver disease (normal AST, ALT, normal CAP, no fibrosis), steatosis (normal AST, ALT, CAP>250, no fibrosis), steato-hepatitis (elevated AST, ALT, CAP>250, no fibrosis) and steato-fibrosis (steato-hepatitis and significant fibrosis on fibroscan kPa > 7). Intestinal Permeability was assessed by measuring both the urinary excretion of the radioactive probe ⁵¹Cr-EDTA, expressed as the percentage of the ingested dose (ID) normalized to creatinine concentration (% ID/g creatinine). mRNA of pro- and anti- inflammatory cytokines such as IL17, IL22, IL1β, TNFα, TGFβ and IL10 was assessed by qPCR in RNA later® preserved duodenal biopsies.

Results : Alcohol-dependent subjects were characterized by an increased intestinal permeability, based on the ⁵¹Cr-EDTA data compared to the controls. Interestingly, intestinal permeability rose progressively with the severity of liver disease (no liver disease < steatosis/steato-hepatitis < steato-fibrosis) Furthermore, the patients with progressive liver disease were characterized by an increase, of the gut specific inflammatory cytokine IL17 compared to alcohol dependent subjects without signs of liver disease, while IL22 did not differ between the different groups. In addition, the gene expression of IL1β, mediator of the innate immune response, increased in subjects with steatosis whereas TNFα did not differ between the different groups. Surprisingly, the anti-inflammatory cytokine IL10 and the pleiotropic cytokine TGFβ, potential inducers of an immune tolerant status, increased in the subjects with steato-hepatitis and steato-fibrosis.

Conclusions : More severe liver disease could be related to higher intestinal permeability. Our results do not favour a predominant pro-inflammatory status of the duodenal mucosa in alcoholic patients as a driver of intestinal permeability. On the opposite, whether alcohol-dependent patients with progressive liver disease develop intestinal immune dysfunction deserves further investigation.

IT ONLY TAKES 25 DAYS TO BUILD A HEPATITIS C CARE NETWORK FOR PEOPLE WHO INJECT DRUGS. W. Verlinden (1), J. Schouten (1), C. Matheï (2), T. Windelinckx (2) / [1] AZ Nikolaas, Sint-Niklaas, Belgium, Gastroenterology and Hepatology, [2] Free Clinic vzw Antwerp, , Belgium, Needle exchange.

Introduction : In Flanders, Belgium, hepatitis C virus (HCV) diagnosis and treatment uptake among people who inject drugs (PWIDs) remain inadequate, despite the existence of evidence-based interventions targeting one or more steps along the HCV care continuum. The existing HCV projects with PWIDs are often initiatives on a local level under the impulse of a few dedicated individuals leading to large inequities in the access to HCV care across the country.

Aim : The goal of this project was to test and optimize methods to increase HCV awareness, diagnosis and linkage to care of PWIDs and to create a practical roadmap for large-scale implementation.

Methods : The project was coordinated by an experienced social worker in Sint-Niklaas, a medium-scale city in Flanders, dedicating one day a week for six months. Firstly, we assessed the current situation, we identified the local needs by interviewing PWIDs, GPs and other social workers and we involved other players such as the local health centre, the justice department and the low threshold drug centre. Secondly, PWIDs were contacted through outreach work and screened through a finger prick test for HCV antibodies. When positive, a standard blood test was performed, followed 2 weeks later by liver elastography and consultation at the hepatology clinic.

Results : 27 PWIDs were approached of which 9 were screened negative, 6 were already followed elsewhere for past/current infection, 2 were recently screened, 1 refused screening and 9 had known positivity for antibodies but were not in medical care. Further evaluation of the HCV antibody positive patients without medical care showed 1 patient with an acute hepatitis, 3 with a past infection (2 treated, 1 spontaneous clearance) and 5 with a chronic hepatitis. Of these last patients, 3 started treatment and 2 didn't meet reimbursement criteria. 1 patient already had liver cirrhosis and hepatocellular carcinoma and received radio frequent ablation before DAA treatment. Most patients were referred from the local drugs centre, justice department and outreach work.

Conclusions : With limited effort, we set up an efficient HCV care network for PWIDs in 25 working days from screening and evaluation to treatment. Social workers play a central role as low barrier contacts for PWIDs and coordinators between the other players in the care cascade. Not only new diagnoses are important, but mostly (re-)introducing known HCV positive PWIDs into medical care. We created a roadmap that can easily be implemented on a national level.

- A37 -

ARE ULTRASOUND SCANS FOR ACUTE SURGICAL ADMISSIONS PERFORMED WITHIN RECOMMENDED 24 HOUR WINDOW? S. Barman (1) / [1] Blackpool Victoria Hospital, United Kingdom (the), General Surgery.

Introduction : RCS Commissioning guide on Emergency Surgery 2014 stated that abdominal ultrasound (USS) is fundamental to the assessment of acute abdominal pain and is of particular utility in the evaluation of biliary, gynaecological and renal pathology or the identification of collections. According to NHS seven-day clinical standard, seven-day access to ultrasound is required with dedicated slots for emergency surgical admissions.

Aim : The primary aim of the study is to determine whether acute ultrasound scans are being performed within 24 hour period. Secondary aims are to find out discrepancies between requests to scan time and day of the week scan was requested and whether US scans were requested following trust guideline.

Methods : A total of 67 patients who had an ultrasound scan within 48 hours of admission to SAU were audited retrospectively from 1st March to 31st July 2018. Scan request times were classified as out of hours if submitted outside the hours of 09:00-17:00 on Weekdays.

Results : Out of 67 acute surgical patients, 40 patients (60%) had USS performed within 24 hour period. Worst performing days were scans requested on Fridays, followed by Tuesdays and Mondays. When US scans were delayed over 24 hours, the length of hospital stay increased from 3.32 days to 5.62 days. All scans were requested following appropriate indications as per trust guidelines. 56 scans (46%) came back with significant finding that might explain the patients symptom. Of those 56 positive scans 33 (58%) were done in <24 hours.

Conclusions : A larger proportion of requested scans do not meet the target when they are requested during normal hours, compared to OOH. Friday is the worst performing day in regards to request of scans. A possible explanation may be no sonography lists being conducted on Saturday afternoon Sundays, leading to a backlog of patients needing scans.

EXPLORING MYELOID CELL HETEROGENICITY IN THE RESOLUTION OF POSTOPERATIVE ILEUS USING SINGLE-CELL RNA SEQUENCING. S. Abdu Rahiman (1), M. Stakenborg (2), V. De Simone (2), S. Ibiza (2), B. Ke (2), D. Pirottin (3), T. Marichal (4), G. Matteoli (2) / [1] KU Leuven, Leuven, Belgium, TARGID, [2] KU Leuven, , Belgium, TARGID, Department of Chronic Diseases, Metabolism and Ageing, [3] University of Liege, Liège, Belgium, Department of Functional Sciences(DSF), [4] GIGA-R, University of Liège, Liège, Belgium, Biochemistry and Molecular Biology.

Introduction : Patients undergoing open abdominal surgery often suffer from a transient episode of intestinal dysmotility referred to as postoperative ileus (POI). Intestinal manipulation (IM) during the surgery evokes tissue damage and consequently an inflammatory response leading to impaired gastrointestinal motility. Recently our lab revealed a critical role for monocyte-derived macrophages (MΦs) in supporting neuromuscular function and restoring intestinal homeostasis after surgical trauma. Blocking monocytes recruitment to the muscularis externa (ME) after IM increased neutrophil-mediated immunopathology and prolong the clinical outcome of POI. Our data indicate that monocyte-derived MΦs acquire essential tissue repair capability essential in restoring intestinal homeostasis and supporting neuromuscular function after surgical trauma.

Aim : Despite significant advances in our understanding of Mφ regulation and function during intestinal inflammation, the factors and the effector molecules responsible for the pro-resolving Mφ-effect remain still not well defined. To answer these questions, we have employed state of the art single cell RNA sequencing (sc-RNA seq) of different subset of intestinal Mφs at the steady state and during the acute and resolution phase of POI. The main goal of our project is to clarify the functions and to investigate the transcription factors and pathways involved in the generation of pro-resolving Mφs during POI.

Methods : Wild-type female mice (WT; C57BL/6J0laHsd) and Csf1rCreERT2/+ Arg1fl/fl were subjected to IM to induce POI. The severity of POI was evaluated by assessing GI transit, and ME inflammation via flow cytometric analysis of recruited immune cells. Immune cells infiltrating the muscularis externa of naïve mice and of mice 1 day and 3 days after IM were isolated by cell sorting analysed by sc-RNA seq. Sc-RNA seq was performed on the Chromium Single Cell Gene Expression Solution (10x Genomics). The 'Seurat' R package was used for graph-based clustering and visualizations. 'SingleR' package was used for immune cell type annotations. Trajectory analysis was performed with 'Monocle2'. Gene set enrichment analysis (GSEA) was done on the average expression of the cell clusters using java GSEA Desktop Application.

Results : Sc-RNAseq of immune cells from the naïve, inflamed and resolving muscularis revealed a complex immune cell landscape during different phases of POI. Resident immune cell populations including muscularis Mφs were seen in naïve ME as expected. At day 1 post IM, myeloid cell infiltration was apparent including mainly monocytes and neutrophils. At day3 post IM, most of the infiltrated myeloid cells seemed to be cleared as the inflammation resolves. The heterogeneity between the myeloid cell types seen on Day1/Day3 go beyond the current understanding by using conventional cell surface marker-based flow cytometry. Trajectory analysis revealed possible differentiation trajectory of classical monocytes to give rise to mature Mφs via multiple intermediate phenotypes. GSEA analysis showed that PPAR-γ targets are differentially upregulated between the cells at the beginning and end of the trajectory hinting at a possible role for PPAR-γ in driving the differentiation of monocytes towards mature Mφs. During this differentiation, the monocyte derived Ly6C low and MHCII low Mφs express the major pro-resolving Mφ factor Arginase 1, a well described PPAR-γ target. Mice lacking Arginase 1 in myeloid cells failed to recover gastrointestinal transit after IM. Hence, the Arg1 expressing myeloid cells could be directly responsible for supporting the recovery of gastrointestinal motility after damage.

Conclusions : Our study reveals a critical role for monocyte-derived Mφs in restoring intestinal homeostasis after surgical trauma. The specific functions of each of these myeloid sub populations has to be further analysed to deepen our understanding of the intestinal inflammatory cascade and the process of resolution of inflammation which could be key in developing novel therapy.

EFFECT OF A BROAD-SPECTRUM SERINE PROTEASE INHIBITOR ON INTRAPERITONEAL ADHESION FORMATION IN A MURINE CAECAL LIGATION AND PUNCTURE MODEL. P. Plaeke (1), J. De Man (1), A. Smet (1), P. Jorens (2), G. Hubens (3), B. De Winter (1) / [1] University of Antwerp, Antwerp, Belgium, Laboratory of Experimental Medicine and Pediatrics, [2] University of Antwerp, Antwerp, Belgium, Laboratory of Experimental Medicine and Pediatrics, Department of Intensive Care Medicine (Antwerp University Hospital), [3] University of Antwerp, Antwerp, Belgium, Antwerp Surgical Training, Anatomy and Research Centre, Department of Abdominal Surgery (Antwerp University Hospital).

Introduction : Intraperitoneal adhesions following abdominal surgery or peritonitis are frequent and are the main cause of intestinal obstruction. Many serine proteases and serine protease inhibitors, involved in the coagulation system and fibrinolysis, have been associated with adhesion formation. Besides they are also considered as potential influencers in intestinal permeability.

Aim : This experimental study aimed to investigate the effect of a single administration of the broad-spectrum protease inhibitor, Nafamostat Mesylate (NFM), on the adhesion formation and intestinal permeability in a caecal ligation and puncture (CLP)-induced sepsis and peritonitis.

Methods : A CLP-procedure with 50% ligation of the caecum and a 21G single puncture was performed in 30 male OF1 mice to induce intraperitoneal adhesions. A vehicle (Aqua, n=8) or NFM at 1mg/kg (n=4), 10mg/kg (n=10), 20 mg/kg (n=8) were intraoperatively administered during the CLP-procedure. For 2 subsequent days, mice were clinically monitored using a validated clinical disease score (Heylen et al.) and they received a saline-glucose solution for fluid resuscitation. On the second day, the abdomen was reopened, adhesion formation was scored and 100µl of 40mg/ml 40 kDa FITC-Dextran solution was in-vivo injected into the ligated small intestine. One hour later, mice were sacrificed and FITC-Dextran was measured in the serum. Adhesions were scored using a composite adhesion score based on the extent of the adhesion formation (adapted from Ezberci et al.), the traction required to separate adhesions, and the time between the abdominal incision and the injection of FITC-dextran in the small intestine at day 2. Data was statistically analyzed using one-way ANOVA with Dunnett's post-hoc test.

Results : During the postoperative period, no significant differences in weight loss (7.50% ±0.97 in the vehicle-treated group versus 9.54% ±0.77 and 8.52% ±0.69 in the NFM 10 mg/kg and NFM 20 mg/kg groups) or clinical disease scores between vehicle-treated and NFM-treated mice were observed. Single administration of NFM 10 mg/kg and NFM 20 mg/kg significantly decreased all subscores of the adhesion score. The extent of the adhesions decreased with 45.2% in the NFM 10 mg/kg group (p<0.001) and 53.7% in the NFM 20 mg/kg group (p<0.001). Additionally, adhesions were better separable with 35.0% (p=0.004) and 37.5% (p=0.003) lower scores in the 10mg/kg and 20 mg/kg treatment group, and the time between incision and the injection of FITC-Dextran decreased with 28.8% (p<0.001) and 33.9% (p<0.001) respectively compared to the vehicle group. Treatment with NFM 1 mg/kg did not significantly reduce adhesion formation. Although administration of NFM tended to reduce intestinal permeability, this reduction was not statistically significant: the permeability of the small intestine was reduced with respectively 47.0% and 40.0% in mice that were treated with NFM at 10 mg/kg and 20 mg/kg compared to vehicle treated mice. Wound healing and coagulation remained unaffected by treatment with NFM. No wound problems or unexpected bleeding were observed.

Conclusions : Single administration of NFM during a CLP-procedure significantly reduced adhesion formation, but did not influence clinical outcomes. The effect on intestinal permeability needs to be studied in more depth.

- B03 -

INTESTINAL BARRIER DYSFUNCTION IN ASSOCIATION WITH FIBROSIS DURING EXPERIMENTAL ACUTE AND CHRONIC COLITIS IN MICE. T. Breugelmans (1), J. De Man (1), B. De Winter (1), A. Smet (2) / [1] Laboratory of Experimental Medicine and Pediatrics, University of Antwerp, Antwerp, Belgium, Faculty of Medicine and Health Sciences , [2] Laboratory of Experimental Medicine and Pediatrics, University of Antwerp, Antwerp, Belgium, Faculty of Medicine and Health Sciences.

Introduction : Inflammatory bowel diseases (IBD), including Crohn's disease and ulcerative colitis, are characterized by perpetual chronic relapsing inflammation of the intestines and intestinal barrier dysfunction is a significant contributor to the pathophysiology of these diseases. Furthermore, chronic inflammation and barrier dysfunction may result in the mucosal and submucosal deposition of the extracellular matrix, which progressively leads to structural fibrosis, a major complication in IBD.

Aim : In this study, we aimed at investigating intestinal inflammation, barrier function and the development of fibrosis using the dextran sodium sulphate (DSS) colitis mouse model.

Methods : Seven-week old C57BL6/J mice were treated with 3 subsequent cycles of 2% DSS in their drinking water for 7 days followed by a recovery phase of 7 days with normal drinking water to induce acute (cycle 1) and chronic colitis (cycle 2 & 3). Control animals received only drinking water. Disease activity was daily monitored based on weight loss, stool consistency and rectal bleeding. At the end of each DSS treatment, groups of mice were used for compliance measurements to investigate the viscoelastic properties of the colon. Thereafter, animals were euthanized and colonic tissue collected to investigate inflammation (H&E), fibrosis (Masson's trichrome), myeloperoxidase (MPO) activity and expression of tight junctions (Cldn1, Cldn2, Ocln, Cdh1, Zo-1, Zo-3), cell polarity proteins (Par3-Par6-aPKC, Crb3) and cytokines (Tnf-α, Il-1β, Il-6, Il-10, Il-22). Intestinal permeability was determined via oral gavage (4h before euthanasia) of 4 kDa FITC-dextran in DSS-colitis and control mice, followed by measuring the fluorescence in the blood. For the experiments, 5-13 mice were included in each group. The scoring of inflammation and fibrosis, MPO activity, intestinal permeability, expression of cytokines and barrier mediators were analysed using a One-Way ANOVA test. The colonic compliance measurements were analysed using a Generalized Estimating Equations test. All data were corrected for multiple testing. P-values below 0.05 were considered to be statistically significant.

Results : Acute colitis in mice was correlated with marked intestinal inflammation, increased expression of several pro-inflammatory cytokines (Tnf- α , Il-1 β and Il-22), increased intestinal permeability, aberrant expression of Cldn1, Cldn2, Zo-3 and Par3 and a remarkable decrease in colonic compliance at lower balloon distension volumes (<80 μ l) compared to healthy control mice. Progression towards chronic colitis resulted in intestinal inflammation with marked bowel wall thickening and fibrotic lesions. Although intestinal permeability was not significantly altered anymore at the end of cycle 2 & 3 of DSS-treatment, barrier mediators, such as Cldn2, Zo-3 and Par3, were still significantly changed in expression compared to healthy control mice.

Conclusions : Colitis progression investigated in the DSS mouse model was associated with intestinal inflammation and barrier dysfunction in the acute phase and the additional development of fibrosis in the chronic phase. The underlying mechanisms involved in barrier dysfunction and existence of fibrosis require further investigation.

- B04 -

AUTOMATIC CELL TRACKING IN CA²⁺ IMAGING RECORDINGS OF THE ENTERIC NERVOUS SYSTEM USING B-SPLINE EXPLICIT ACTIVE SURFACES. Y. Kazwiny (1), W. Boesmans (2), J. Pedrosa (3), J. D'hooge (3), P. Vanden Berghe (1) / [1] KU Leuven, Belgium, TARGID, [2] Hasselt University, Hasselt, Belgium, Dynamici Bioimaging lab, [3] KU Leuven, Belgium, Cardiovascular Imaging and Dynamics.

Introduction : Ca²⁺ imaging is an exceptionally valuable optical microscopy technique to record neuronal activity and investigate neuronal circuitry in complex networks like the enteric nervous system (ENS), which controls intestinal function. Ca²⁺ imaging analysis, however, faces several challenges. Image quality limitations such as low SNR and out-of-focus frames plague recordings produced with this technique. These limitations, which are often unavoidable because of biological reasons, greatly limit the applicability of common segmentation techniques.

Aim : Practically, manual delineation such as marking spatially static regions of interest (ROIs) is still the prominent method used to extract the average pixel-intensities and derive Ca²⁺ signals from recordings. This procedure is time-consuming and often not applicable. For instance, if cells move or tissues deform, no static ROI can contain all cell-belonging pixels in every frame of the recording. Rigid registration techniques struggle against some contraction related tissue movement and the rapid temporal intensity changes of cell-belonging pixels. Therefore, there is a need for accurate cell tracking that allows to track cells in moving frames and is insensitive to large intensity changes in consecutive recording frames.

Methods : We propose a novel method based on a B-Spline Explicit Active Surfaces (BEAS) framework that delineates neuronal cell bodies and tracks them during tissue movement. In this algorithm, semi-automatic cell detection is initiated in/from a brief static scene and detection is based on a combination of morphological operations including distinguished features of neurons expressing a genetically-encoded Ca²⁺ indicator. For the BEAS algorithm, every cell is represented by an active contour whose development depends on local energy terms at every node of the contour and global energy terms such as curvature, size, and size differential between frames. The contours are coupled using additional competition penalties that represent cells competing for space throughout the recording.

Results : We exploit the distinct dark appearance of nuclei specific to popular Ca²⁺ sensors by creating a coupled two-layer segmentation mode that tracks a nucleus' boundaries as well as the cytoplasmic contour and optimizes the two layers together to obtain a stable shape throughout recordings.

Conclusions : We provide this algorithm as a Matlab package that caters to specific needs for live cell Ca²⁺ imaging analysis. In addition to the tracking algorithm, the package introduces a robust technique for tracking manual ROIs throughout the most challenging recordings by extrapolating the geometric transformation representing the movement from the cell contours that were tracked successfully. Compared to manual delineation and other segmentation methods the proposed algorithm is able to track cells during relatively large tissue deformations and high-intensity changes such as during neuronal firing events. Our analysis package represents a significant improvement to available Ca²⁺ imaging analysis workflows.

- B05 -

CATHEPSIN S-MEDIATED ACTIVATION OF HUMAN MAS-RELATED G PROTEIN-COUPLED RECEPTOR F: A STORY OF AN UNDERRATED ROLE FOR CYSTEINE PROTEASE(S) IN INFLAMMATORY BOWEL CONDITION? R. Arora (1), S. Van Remoortel (1), G. Van Raemdonck (2), G. Baggerman (2), R. Buckinx (1), D. Snyders (3), A. Labro (3), J. Timmermans (1) / [1] Laboratory of Cell Biology and Histology, Department of Veterinary Sciences, University of Antwerp, Antwerpen, Belgium, Veterinary Sciences, [2] University of Antwerp, Antwerp, Belgium, Laboratory of Systemic Physiological & Ecotoxicological Research, Department of Biology, [3] University of Antwerp, Antwerp, Belgium, Laboratory for Molecular, Cellular and Network Excitability, Department of Biomedical Sciences.

Introduction : The superfamily of seven-transmembrane domain receptors (7TMRs) also called as G protein-coupled receptors (GPCRs) regulate a wide array of physiological processes in both healthy and diseased conditions via canonical and non-canonical signaling pathways. A subfamily of class A GPCRs, Mas-related G protein-coupled receptors (MRGPRs), is predominantly expressed in sensory neurons of the dorsal root and trigeminal ganglia, as well as on mast cells. Interestingly, we recently discovered that Mas-related G protein-coupled receptor F (MRGPRF), which is known to be expressed by brain, spinal cord and enteric neurons, is also expressed by enteroendocrine cells in the gastrointestinal tract. MRGPRF expression was predominantly found at basal and basolateral sites, indicating a novel role in endocrine regulation. Additionally, we discovered that the cysteine protease Cathepsin S (Cat-S) is predominantly expressed by macrophages in vicinity to enteroendocrine cells, possibly indicative of a potential role of Cat-S in activation of MRGPRF.

Aim : To unravel the molecular interactions between MRGPRF and Cat-S.

Methods : We first performed in-silico analysis of the N-terminal sequence of MRGPRF, which revealed consensus motif sites of cleavage by Cat-S. Firstly, luciferase tagged at the N-terminus of MRGPRF expressed in HeLa cells was incubated with Cat-S and receptor N-terminal cleavage was assessed by measuring luminescence activity in the supernatant. Furthermore, the N-terminal end of MRGPRF was synthesized, incubated with Cat-S and analyzed for cleaved sites using mass spectroscopy. We next determined receptor activation upon Cat-S treatment using live cell calcium imaging with Fluo-4.

Results : The high luciferase activity in the supernatant compared to its control (no Cat-S treatment) indicated cleavage of the N-terminal end of MRGPRF. The mass spectroscopy results clearly showed cleavage sites on the N-terminal end of the peptide and as such corroborated with in-silico analysis. Live cells imaging showed that HeLa cells transfected with MRGPRF and incubated with Cat-S, gave rise to transient calcium fluxes when compared to controls (non-transfected HeLa cells), indicative of protease-based receptor activation.

Conclusions : The observed cleaving activity of Cat-S on MRGPRF, together with the demonstrated morphological association of Cat-S expressing macrophages and MRGPRF-expressing neurons and enteroendocrine cells might pave the way for deorphanization of MRGPRF and call for further pathological investigations on this Cat-S/MRGPRF interaction, in particular regarding its involvement in neuro-immune communication within the healthy and inflamed gut. Support or Funding Information: This study supported by research grant G019314N of the Research Foundation-Flanders (FWO) and by a DOCPRO1 BOF grant 34867 of the University of Antwerp, Belgium.

- B06 -

GHRELIN AS A MEDIATOR OF METABOLIC PROGRAMMING OF OBESITY AFTER UNDERNUTRITION. S. Sun (1), K. Corbeels (2), D. Louis (3), A. Segers (3), Q. Wang (3), B. Van Der Schueren (4), I. Depoortere (3) / [1] KU Leuven, , Belgium, TARGID Gut Peptide Research Lab, [2] KU Leuven, Leuven, Belgium, Clinical and Experimental Endocrinology, [3] KU Leuven, Belgium, TARGID Gut Peptide Research Lab, [4] KU Leuven, Belgium, Clinical and Experimental Endocrinology.

Introduction : Maternal undernutrition triggers persistent changes in the function of hypothalamic circuits to adapt to the prospective life conditions. When a mismatch occurs between prenatal conditions and the later-life environment there is an increased risk of developing diseases.

Aim : Since the hunger hormone ghrelin has been shown to control neural fiber growth of the hypothalamus during postnatal life, we hypothesize that the high ghrelin levels during maternal undernutrition affect the development of the hypothalamus and induce lifelong metabolic changes.

Methods : Pregnant C57BL/6J mice (11 weeks) were assigned to either a normal nourished (NN) group, fed a standard diet (SD) throughout gestation, or an undernutrition (UN) group, fed 70% of the food consumed by the NN group from 10 days postcoitum to the day of delivery. All pups were fostered by NN mice. Pups were sacrificed at postnatal day 10 (P 10), P 15 and P 21 and ghrelin was measured in plasma samples and gastrointestinal tissue extracts by radioimmunoassay. For the long-term study, male offspring from either NN or UN group were fed after weaning a SD until week 8, followed by a HFD until week 17. At week 13, an oral glucose tolerance test (OGTT) was performed and at week 15 metabolic changes were measured in Calocages (TSE systems). Mice were sacrificed at week 17.

Results : At birth, body weight was lower ($P < 0.05$) and body length was shorter ($P < 0.001$) of UN pups compared to NN pups. After fostering, UN pups already caught-up their body weight ($P < 0.05$) and growth ($P < 0.001$) at P 2 and this effect persisted during the first 3 weeks. During the postnatal period, a steep increase ($P < 0.001$) in plasma ghrelin levels was observed in both groups between P 10 and P 15 and a decrease between P 15 and P 21. The age-dependent changes in plasma ghrelin during the postnatal period correlated in both groups with changes in stomach but not duodenal ghrelin tissue content, indicating that the stomach is the source of the surge in plasma ghrelin levels. LEAP2 duodenal mRNA expression, the endogenous ghrelin receptor antagonist, correlated with the changes in plasma ghrelin levels in the NN group but not in the UN group. Age-dependent changes in hypothalamic AgRP mRNA expression were observed in the NN pups which paralleled plasma ghrelin levels but not in the UN pups which showed an increase in POMC mRNA expression. After weaning with a SD, no difference in food intake and body weight was observed between

both groups until week 8. After feeding a HFD from week 9, UN mice ate more ($P<0.05$) and gained more weight ($P<0.001$) than NN mice. No difference in glucose intolerance was observed between both groups at week 13. At week 15, oxygen consumption ($P<0.05$) and heat production ($P<0.05$) were more pronounced in UN pups. Locomotor activity and respiratory exchange rate did not differ between both groups. At week 17, daily food intake (+13%) ($P<0.05$) and body weight (+21%) ($P<0.01$) of UN pups was increased compared to NN pups.

Conclusions : A mismatch between the predicted environment during pregnancy (undernutrition) and later-life environment (high-fat nutrition) promotes the susceptibility to develop obesity.

- B07 -

LONG TERM EFFECTS OF FECAL MICROBIOTA TRANSPLANTATION IN IRRITABLE BOWEL SYNDROME WITH PREDOMINANT ABDOMINAL BLOATING: RESULTS FROM A DOUBLE BLIND, PLACEBO-CONTROLLED, RANDOMIZED CONTROLLED TRIAL. T. Holvoet (1), E. Christiaens (1), M. Joossens (2), J. Boelens (3), B. Verhasselt (3), M. De Vos (1), P. Hindryckx (1), J. Raes (2), D. De Looze (1) / [1] UZ Gent, Gent, Belgium, Gastroenterology, [2] KU Leuven, Belgium, Microbiology, [3] UZ Gent, Gent, Belgium, Microbiology.

Introduction : Intestinal microbiota dysbiosis is thought to play an important role in the pathophysiology of irritable bowel syndrome (IBS), especially in those patients with severe abdominal bloating [1,2]. Fecal microbiota transplantation (FMT) is effective in correcting this gut microbiota imbalance and has been previously shown as an effective treatment strategy in these patients [3,4]. However, no data are available about effect duration and relapse rates.

Aim : However, no data are available about effect duration and relapse rates.

Methods : Long term follow-up data after 1 year were collected from a double-blind, placebo-controlled randomized, single-centre clinical trial. Briefly, patients with refractory IBS symptoms and predominant abdominal bloating (defined by the ROME III criteria), aged 18-75 years and without constipation were included and randomly assigned (2:1) to transplantation with fresh donor stool or placebo (patient's own frozen stool). Donors (N=2) were selected based on both having a rich microbial diversity and showing good clinical results in a preliminary pilot trial [4]. They were screened for infectious diseases on a regular base (HAV, HBV, HCV, HIV, Treponema in blood, enteropathogens, Clostridium difficile toxin and parasites in stools). Transplants were prepared as previously described [4] and administered through a nasojejunal tube which was placed electromagnetically guided (Cortrak). Patients were contacted 6 months and one year after transplantation to evaluate long term success defined as self-reported improvement of overall IBS symptoms and abdominal bloating in particular. This study is registered on ClinicalTrials.gov (NCT02299973).

Results : Between December 2015 and September 2017, a total of 62 IBS patients was randomized to active donor treatment (N= 42) or placebo (N=22) with a positive response at twelve weeks in respectively 49% and 29% of patients ($P=0.004$). Long term data were available in 53 patients (85%). Of the 22 patients who had an initial response, only 6 (27%) reported lasting improvement one year following FMT, with 73% experiencing a relapse of abdominal symptoms. One patient with long term improvement received placebo treatment, the others were included in the active treatment arm. Interestingly, the majority of long-lasting responders (4/5, 80%) received stools from the same donor.

Conclusions : Although FMT appears to be an effective treatment for IBS patients with abdominal bloating, positive effects are short-lived in most patients. Further studies should focus on frequency and timing of FMT administration.

- B08 -

EVIDENCE OF TRANSCRIPTIONAL CHANGES IN PATHWAYS REGULATING 5-HT RELEASE FROM ENTEROCHROMAFFIN CELLS IN IRRITABLE BOWEL SYNDROME. A. Denadai-Souza (1), N. Fabre (1), J. Aguilera-Lizarraga (1), L. Decraecker (1), A. Beyder (2), G. Boeckxstaens (1) / [1] KU Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing, [2] Mayo Clinic, Rochester, United States (the), Departments of Medicine and Physiology & Biomedical Engineering.

Introduction : Mounting evidence indicates that enterochromaffin (EC) cells are prime cellular mediators of irritable bowel syndrome (IBS) pathophysiology. Indeed, EC cells express a unique repertoire of chemo- and mechanosensory receptors regulating release of serotonin (5-hydroxytryptamine, 5-HT), a pivotal mediator of many gastrointestinal functions closely related to IBS symptoms, such as motility, fluid secretion and sensation. Accordingly, the number of EC cells and the level of 5-HT in the mucosa and in postprandial plasma are altered in IBS patients, and particularly increased in IBS-D. Conversely, 5-HT₃ receptor antagonists significantly improve abdominal pain in 50% of IBS-D patients, although most were withdrawn from the market due to rare yet serious side effects. Herein, we hypothesized that the identification of dysregulated upstream pathways underlying aberrant 5-HT release from EC cells would pave the way to new therapeutic strategies for IBS.

Aim : To profile transcriptional disturbances to upstream pathways implicated in 5-HT release in IBS.

Methods : Reference genes for IBS have not been thoroughly validated, therefore we initially screened for the most

stable genes across microarray databases of 347 colorectal human samples of healthy volunteers and IBS patients (Affymetrix 133 Plus 2 Arrays) by using the RefGenes tool from the GeneInvestigator Bioinformatics Suite (Nebion; Switzerland). Hence, specific oligonucleotides to reference gene candidates (identified by RefGenes tool or often reported in IBS and inflammatory bowel disease literature), as well as to target genes from pathways implicated in 5-HT release were designed by using the RealTime qPCR tool (Integrated DNA Technologies, USA). Stability and disturbances in expression of reference and target genes was investigated by RT-qPCR with cDNA libraries synthesized from total RNA extracted from rectal mucosa biopsies (healthy volunteers, n=15; IBS-C, n=11; IBS-D, n=15). The most stable combination of reference genes was validated with the Office Excel Add-in GeNorm v3. Relative expression of genes from 5-HT releasing pathways was calculated by using the $\Delta\Delta C_t$ method. Data was expressed as fold change relative to healthy volunteer samples and compared statistically with Kruskal-Wallis followed by multiple comparisons with Dunn's test. A fold change >1.5 and a $p < 0.05$ was considered as significant.

Results : Among reference gene candidates spotlighted by our approach, a pair-wise analysis with GeNorm indicated a geometric mean of RPS11 and TMSB10 as the most stable configuration for healthy volunteers and IBS. Hence, the analysis of expression relative to RPS11/TMSB10 identified an upregulation of multiple genes implicated in 5-HT synthesis, transport and secretion, such as adrenergic, olfactory and mechano-transduction pathways. Furthermore, these changes were particularly enriched in IBS-D. The identity of specific genes within these pathways cannot be disclosed yet as a patentability check is being performed.

Conclusions : Herein, we identified and validated the first set of reference genes to study relative expression in the colorectal mucosa of IBS patients. Based on our robust approach, we highlighted that major pathways implicated in 5-HT release from EC cells are upregulated in IBS-D, further supporting the translational potential of our hypothesis. Follow-up assays based on multiplexed single molecule fluorescence in situ hybridization and immunofluorescence will support these findings with added spatial resolution.

- B09 -

PSYCHOLOGICAL STRESS TRIGGERS A BYSTANDER IMMUNE RESPONSE TO FOOD ANTIGENS LEADING TO NEURONAL HYPEREXCITABILITY AND VISCERAL HYPERSENSITIVITY. J. Aguilera-Lizarraga (1), M. Florens (1), C. Lopez-Lopez (2), J. Jaramillo-Polanco (2), S. Vanner (2), D. Reed (2), M. Wouters (1), G. Boeckxstaens (1) / [1] KU Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing, [2] Queen's University, Kingston, Ontario, Canada, Kingston, Canada, GI Diseases Research Unit.

Introduction : The two most characterized triggers for the development of irritable bowel syndrome (IBS) are an episode of bacterial gastroenteritis and psychological stress. Increased colonic permeability induced by stress facilitates the entrance of luminal antigens and has been linked with disturbances in the immune response. However, how this leads the development of visceral hypersensitivity (VHS) remains poorly understood. Of interest, we previously showed that the exposure to food antigens (such ovalbumin, OVA) during a gastrointestinal infection breaks the development of oral tolerance triggering an adaptive immune response. Later re-exposure to these food antigens results in mast cell activation and development of VHS. Here, we hypothesized that, similar to a gastrointestinal infection, psychological stress triggers an aberrant immune response to dietary antigens leading to VHS upon re-exposure.

Aim : To evaluate whether psychological stress may break the development of oral tolerance and lead to food-mediated development of VHS.

Methods : BALB/c mice (n=9-13/group) were subjected to repeated water-avoidance-stress (WAS) or sham stress (shamWAS) for 10 consecutive days and exposed to OVA or saline (OVA-WAS, OVA-shamWAS, saline-WAS; respectively). After 5 weeks, all mice were re-exposed to OVA by oral gavage. After 8 OVA challenges, OVA-WAS mice were randomized to one week treatment with either doxantrazole (mast cell-stabilizer) or vehicle. Visceral pain was assessed by recording of the visceromotor response to colorectal distension using abdominal muscle electromyography before and at 2, 4, 6 and 7 weeks post-stress, and after doxantrazole treatment. Thereafter, colonic tissues were collected and stored in RNAlater to assess expression of inflammatory markers by qPCR. Also, colonic tissues were incubated in RPMI medium and supernatant were collected. Neuronal excitability (n=23-24) was evaluated using patch clamp recording in DRG neurons incubated with colonic supernatants. The involvement of H1R was tested using its antagonist pyrillamine.

Results : WAS, but not shamWAS, triggered a short-lasting period of VHS ($p=0.001$), returning to normal after 4 weeks. Of note, repeated oral gavage with OVA triggered VHS in OVA-WAS mice ($p=0.0001$), but not in OVA-shamWAS or saline-WAS mice. Doxantrazole-treatment normalized the increased pain perception in OVA-WAS mice after OVA re-exposure ($p=0.041$). OVA-WAS mice displayed an increased colonic gene expression of Tryptase α/β -1 and Kit ($p < 0.05$) and downregulation of *Infy*, *Il1 β* , *Ccl2* and *Il10* ($p < 0.05$) compared to OVA-shamWAS mice. Colonic supernatant of OVA-WAS mice reduced neuronal rheobase ($p < 0.02$) and increased the number of action potentials at 2x rheobase ($p < 0.05$) compared to supernatants from OVA-shamWAS and saline-WAS mice, indicating neuronal hyperexcitability. These effect was mediated via H1R, as pyrillamine reversed the effect of OVA-WAS supernatants on the rheobase

(p=0.005).

Conclusions : These data indicate that, similar to an infectious gastroenteritis, psychological stress can also promote the break of oral tolerance to dietary antigens and lead to mast cell-induced VHS upon antigen ingestion. This is induced by neuronal hyperexcitability mediated by H1R activation.

- B10 -

MAS-RELATED G PROTEIN-COUPLED RECEPTOR C11 (MRGPC11) AND ITS HUMAN ORTHOLOGUE MRGPRX1: NOVEL PLAYERS IN VISCERAL HYPERSENSITIVITY? S. Van Remoortel (1), H. Ceuleers (2), R. Arora (1), L. Van Nassauw (3), J. De Man (2), R. Buckinx (1), B. De Winter (2), J. Timmermans (1) / [1] Laboratory of Cell Biology and Histology, Department of Veterinary Sciences, University of Antwerp, Antwerpen, Belgium, Veterinary Sciences, [2] Laboratory of Experimental Medicine and Pediatrics, Faculty of Medicine and Health Sciences, University of Antwerp, Wilrijk (Antwerp), Belgium, , Belgium, Medicine, [3] Laboratory of Human Anatomy and Embryology, Faculty of Medicine & Health Sciences, University of Antwerp, Antwerpen, Belgium, Medicine.

Introduction : Visceral hypersensitivity is a hallmark feature of IBD and IBS and typically presents as an increased pain perception from the bowel. It is believed that aberrant nociceptive signaling through multiple receptors and ion channels can induce long-term sensitization of gut afferents, contributing to an increased sensitivity to mechanical stimulation of the bowel. Despite these insights, the pathogenesis of visceral hypersensitivity still remains poorly understood. Since their first description in the early 2000's, the family of Mas-related G protein-coupled receptors (Mrgpr) have emerged as novel targets in pain research. Especially for the murine MrgprC11, several recent studies have indicated that this receptor plays an important role in the neurobiology of nociception in skin and airways. The role of MrgprC11 in visceral nociception is currently unexplored.

Aim : We aimed to study the presence of MrgprC11 and MRGPRX1 in the mouse and human gut nociceptive pathways respectively and to investigate whether MrgprC11 is capable to modulate visceral sensitivity in healthy mice.

Methods : Immunohistochemistry for MrgprC11 was performed on cryosections of murine DRGs retrogradely labeled from the distal colon. In addition, after noxious colo-rectal balloon distention (CRD) (70mmHg), immunoreactivity for pERK1/2 was compared in spinal dorsal horn neurons (T11-L2) of mice that received the MrgprC11 ligand (BAM8-22) and of mice that received vehicle (saline) intracolonicly. To further assess the effect of intracolonic BAM8-22 on visceral sensitivity, the visceromotor response (VMR) to graded CRD (15mmHg, 30mmHg, 50mmHg and 70 mmHg) was determined. Expression of inflammatory cytokines and MPO activity were evaluated to determine whether BAM8-22 induces colonic inflammation. Using in situ hybridization on human thoracolumbar DRGs, we determined the presence of MRGPRX1, the human orthologue of MrgprC11, in human DRG neurons.

Results : MrgprC11 was expressed by a proportion of colon-innervating mouse DRG neurons. Preliminary data indicate that intracolonic BAM8-22 increases the number of pERK1/2-immunoreactive dorsal horn neurons after noxious CRD. Furthermore, BAM8-22-treated mice showed significantly increased VMR at 30mmHg and higher compared to vehicle-treated mice, an effect that was abolished in Mrgpr cluster KO mice lacking MrgprC11 expression. Visceral hypersensitivity was not due to colonic inflammation, as inflammatory parameters were similar between BAM8-22-treated and vehicle-treated mice. In human thoracolumbar DRG's, we were able to demonstrate the neuronal expression of MRGPRX1.

Conclusions : Our results indicate that MrgprC11 is expressed in visceral nociceptive pathways and that colonic single administration of its ligand BAM8-22 induces visceral hypersensitivity in mice. Furthermore, we show for the first time that the human counterpart of MrgprC11, i.e. MRGPRX1, is expressed in human thoraco-lumbar DRG neurons. These data support our hypothesis that MrgprC11 is a valid target with regard to visceral hypersensitivity and warrant further research on its possible role in gastro-intestinal disorders such as IBD and IBS. This study was supported by research grant G019314N of the Research Foundation-Flanders (FWO).

- B11 -

ESTROGENS MODULATE THE EFFECT OF STRESS ON COLONIC SENSITIVITY AND FUNCTION IN A SPONTANEOUS RAT MODEL OF FUNCTIONAL GASTRO-INTESTINAL DISORDERS. A. Accarie (1), J. Toth (1), L. Wauters (1), R. Farré (1), J. Tack (1), T. Vanuytsel (1) / [1] KU Leuven, Belgium, Translational Research Center for Gastrointestinal Disorders.

Introduction : Functional gastro-intestinal disorders (FGID) such as IBS and FD are more prevalent in women than in men with a ratio of 2:1. Furthermore, stressful life events were reported as one of the triggers for FGID symptoms in patients. Recently our group identified the normoglycemic diabetes prone BioBreeding rat (BBDP rat) as a spontaneous model of FGID with increased jejunal permeability, immune cells infiltration and visceral hypersensitivity in the colon (Meleine, DDW 2017) in both males and females, but more pronounced in the latter. We also demonstrated stress-

induced visceral hypersensitivity in females only (Accarie, DDW 2018). In this study we aimed to investigate the role of estrogens in GI symptoms at baseline and after maternal separation.

Aim : In this study we aimed to investigate the role of estrogens in GI symptoms at baseline and after maternal separation.

Methods : Newborn female rats were separated from the dams from day 2 to 15, 3 hours per day. Control animals were not handled until the weaning. Anxiety levels were determined with the marble burying test before testing the colonic sensitivity, which was assessed before and two weeks after ovariectomy (ovx; 8/group) by measuring the visceromotor response (VMR) to isobaric (15, 30, 45 and 60 mmHg) rectal distensions corrected to wall tension according to Laplace's law. Two days after the sensitivity test rats were euthanized and tissue was mounted in Ussing chambers after removal of the muscle layer. Epithelial integrity was evaluated using cumulative transepithelial passage of fluorescein isothiocyanate-dextran of 20kDa (jejunum) or 4 kDa (colon) over 120 min. Mast cell and eosinophil density in the lamina propria were quantified by Mast Cell Protease type 2 immunostaining or Chromotrope 2R staining respectively.

Results : In non-stressed conditions, ovariectomy affected jejunal (598.4 ± 167.3 (sham) vs 252.4 ± 71.2 (ovx) pmol/cm² n=6 p=0.05) and colonic barrier function (65.4 ± 13.4 (sham) vs 308.7 ± 108.1 (ovx) pmol/cm² n=6 p=0.03) and induced an increase of immune cell density in the jejunum and a decrease in the colon while colonic sensitivity and anxiety were unaltered. In contrast, the exposure to an early life stress resulted in an increased VMR in female rats, suggesting colonic hypersensitivity, which was abolished after ovariectomy (p<0.01). In the same way, the increased number of marbles buried, reflecting anxiety, was reduced after ovariectomy (5.8 ± 1.3 vs 2.5 ± 0.7 p=0.05). However, the increased immune cells infiltration in the colonic and jejunal epithelial and permeability in both regions remained unaltered after ovariectomy.

Conclusions : Our results point out a different role for estrogens on FGID pathogenesis under stress and non-stress conditions. These observations highlight the necessity to focus on female animals in the context of FGID and stress-related alterations and further validate the BB-rat as an attractive model to characterize the gender-dependent pathophysiology of FGID.

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SERINE PEPTIDASES AS NOVEL TARGET TO TREAT VISCERAL HYPERSENSITIVITY. L. Decraecker (1), B. De Winter (2), V. Cacheux (3), K. Augustyns (3), A. Denadai-Souza (1), G. Boeckxstaens (1) / [1] KU Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing, [2] University of Antwerp, Antwerp, Belgium, Department of Gastroenterology and Hepatology, [3] University of Antwerp, Antwerp, Belgium, Department of Pharmaceutical Sciences.

Introduction : Visceral hypersensitivity (VHS), mediated by the sensitization of colorectal sensory afferents, underlies abdominal pain in irritable bowel syndrome (IBS). Strong evidence indicates that sensitization of transient receptor potential (TRP) channels on the nerve endings of these colorectal nociceptors results in increased visceral pain perception. Indeed, our group highlighted the presence of sensitized TRPV1, TRPV4 and TRPA1 channels in almost 80% of IBS patients. Mediators that are involved in symptom generation in IBS are poorly understood, but increasing evidence supports a pivotal role for peptidases and Peptidase-Activated Receptors (PARs). Peptidases released by colonic tissue from IBS patients have been shown to cause VHS in animal models and failed to do so in animals lacking PARs. Studies have also demonstrated increased proteolytic activity of serine peptidases in mucosal tissue of IBS patients. Nevertheless, the identity of dysregulated serine peptidases as well as molecular mechanisms implicated in IBS remain elusive.

Aim : We first aim to characterize the subclass of serine peptidases that is overactive in IBS patient samples. Based on these results we will later precisely identify overactive peptidases by functional proteomics. Additionally, a novel serine peptidase inhibitor (UAMC-00050) has been shown to abrogate VHS in pre-clinical models of VHS. Herein, we aim to further exploit the translational potential of UAMC-00050 by assessing its inhibitory activity towards serine peptidase activity released by rectal mucosa supernatants.

Methods : Rectal mucosa biopsies were collected in ice-cold oxygenated Krebs buffer and transferred immediately to a serum-free cell culture medium. The samples were incubated for 1h and 24h at 37°C after which the supernatants (SN) was collected and stored at -80°C until analysis. The activity of the three serine peptidase subclasses (trypsin-, chymotrypsin- and elastase-like) was quantified with a microplate reader, using subclass-specific enzymatic substrates. Similarly, the inhibitory activity of UAMC-00050 was measured by enzyme kinetics.

Results : A subpopulation of IBS patients presented a clear increase in trypsin-like activity compared to healthy subjects both in the SN collected at 1h as well as at 24h. Activity levels of chymotrypsin- and elastase-like serine peptidases were low and similar between healthy volunteers and IBS patients. The compound UAMC-00050 inhibited the trypsin-like activity released from pooled rectal mucosa supernatants from IBS patients (IC₅₀ = 72 nM). Hence, UAMC-00050 at 100 nM inhibited trypsin-like activity in supernatants from individual subjects, bringing activity levels down to the level observed in samples from healthy volunteers.

Conclusions : We can conclude that among serine peptidases, trypsin-like peptidases are most likely involved in symptom generation in IBS patients as their activity shows a clear increase in a significant subpopulation of IBS patients.

Moreover, a low concentration of the serine peptidase inhibitor that has demonstrated efficacy in pre-clinical models of VHS, inhibits trypsin-like activity released by rectal mucosa biopsies from IBS patients. To get further insights on the mechanism by which the compound UAMC-00050 inhibits VHS, we will assess its impact on TRP channel sensitization triggered by incubation of human cells with supernatants from IBS patients.

- B13 -

LOCAL RECTAL ADMINISTRATION OF A SERINE PROTEASE INHIBITOR REVERSES VISCERAL HYPERSENSITIVITY IN A RAT MODEL FOR IRRITABLE BOWEL SYNDROME

N. Hanning (1), H. Ceuleers (1), M. De Bruyn (2), I. De Meester (2), J. Joossens (3), K. Augustyns (3), H. De Schepper (1), A. Smet (1), J. De Man (1), B. De Winter (1) / [1] University of Antwerp, Antwerp, Belgium, Laboratory of Experimental Medicine and Pediatrics, division of gastro-enterology, [2] University of Antwerp, Antwerp, Belgium, Laboratory of Medical Biochemistry, [3] University of Antwerp, Antwerp, Belgium, Laboratory of Medicinal Chemistry.

Introduction : Serine proteases are enzymes present at high levels in the gastrointestinal tract and have been implicated in the pathophysiological mechanisms underlying several gastrointestinal disorders. Selective inhibition of these serine proteases has been suggested as a new therapeutic strategy in the treatment of visceral pain in Irritable Bowel Syndrome (IBS). Previously, we demonstrated beneficial effects of a single intraperitoneal administration of UAMC-00050, a serine protease inhibitor with a well-known inhibitory profile developed at our university (patent WO2007045496, WO2017198753), on visceral hypersensitivity in a 2,4,6-trinitrobenzenesulfonic acid (TNBS)-colitis post-inflammatory rat model for IBS (Ceuleers et al., BJP 2018).

Aim : The aim of this study was to acquire more preclinical knowledge regarding the delivery mode of this compound by investigating the effect of the local administration of UAMC-00050 in the colorectum.

Methods : At day 0, a TNBS enema (4 mg, in 50% ethanol) was used to induce a mild colitis in adult male Sprague-Dawley rats. Control animals received an enema with 0.9% NaCl. The presence of colitis was confirmed by colonoscopy at day 3. From day 10 onwards, the colonoscopy was repeated every 4 days until mucosal healing was observed. Three days after the resolution of colitis, the serine protease inhibitor UAMC-00050 (1 – 5 mg/kg) or its vehicle was administered intra-rectally under isoflurane anesthesia. Thirty minutes later, visceral sensitivity was examined by quantifying the visceromotor response (VMR) to increasing colorectal distension pressures (10 – 60 mmHg, 20 s, 4 min interval), expressed as an integral of the electromyographic response (EMR; $\mu\text{V}/20\text{s}$) for visceral allodynia (10 – 30 mmHg) and hyperalgesia (40 – 60 mmHg). Afterwards, we assessed colonic compliance in vivo by introducing a balloon through the anus and applying graded volumes of water while measuring intraballloon pressure (0 – 2 mL, 80 s interval) under pentobarbital anesthesia. Finally, the inflammatory parameters (colonoscopy, macroscopy, microscopy and myeloperoxidase activity) were scored to confirm the post-inflammatory status at the day of the VMR and compliance measurements.

Results : At day 3, rats treated with TNBS showed signs of a mild colitis, indicated by significantly increased colonoscopic scores compared to control animals (6.83 ± 0.32 , $n = 24$ vs. 0.00 ± 0.00 , $n = 7$). At the day of the VMR and compliance experiments, the post-inflammatory status of the rats was confirmed by colonoscopic, macroscopic and microscopic scoring, as well as by measuring the myeloperoxidase activity. In sensitivity experiments, both control animals and vehicle-treated post-colitis rats showed gradually increasing VMRs but VMRs were significantly higher in post-colitis rats, indicating the presence of visceral hypersensitivity in these animals. Post-colitis rats displayed signs of both allodynia (10 – 30 mmHg, total EMR: 882.13 ± 145.45 vs. 279.63 ± 51.48 , $n = 8$, $p < 0.001$) as well as hyperalgesia (40 – 60 mmHg, total EMR: 1857.75 ± 265.39 vs. 738.50 ± 114.88 , $n = 8$, $p < 0.001$). Intrarectal treatment with a low dose of UAMC-00050 (1 mg/kg) resulted in a significant amelioration of the allodynia (10 – 30 mmHg, total EMR: 524.50 ± 97.93 vs. 882.13 ± 145.45 , $n = 8$, $p < 0.05$), but not the hyperalgesia (40 – 60 mmHg, total EMR: 1503.38 ± 284.59 vs. 1857.75 ± 265.39 , $n = 8$). Intrarectal treatment with a high dose of UAMC-00050 (5 mg) resulted in a significant decrease of both the allodynia (10 – 30 mmHg, total EMR: 132.25 ± 66.63 vs. 882.13 ± 145.45 , $n = 8$, $p < 0.001$) and hyperalgesia (40 – 60 mmHg, total EMR: 417.13 ± 133.41 vs. 1857.75 ± 265.39 , $n = 8$, $p < 0.001$). Post-colitis animals treated with vehicle displayed a colonic compliance similar to control animals, while post-colitis animals treated with UAMC-00050 in a high dose (5 mg/kg) showed a higher compliance.

Conclusions : Our results confirm the beneficial effects of the serine protease inhibitor UAMC-00050 on visceral hypersensitivity in a post-inflammatory rat model for IBS and additionally show that the serine protease inhibitor is also effective when administered locally in the rectum. A local effect of the compound on the colonic compliance could contribute to these beneficial effects. The outcome of this study thereby expands the evidence regarding the use of serine protease inhibitors for the treatment of visceral pain in IBS patients.

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RVD2 AS POTENTIAL NEW TREATMENT FOR VISCERAL HYPERSENSITIVITY IN IBS. M. Florens (1), E. Perna (2), J. Aguilera-Lizarraga (2), S. Theofanous (2), M. Wouters (2), G. Boeckxstaens (2) / [1] University Hospitals Leuven, Leuven, Belgium, TARGID, [2] University Hospitals Leuven, Belgium, TARGID.

Introduction : Sensitization of TRPV1 was recently implicated in visceral hypersensitivity (VHS) in patients suffering from the irritable bowel syndrome (IBS). Resolvins (Rv), including RvD1, RvD2 and RvE1 are endogenous mediators essential for the resolution of an inflammatory response that also display analgesic effects. In somatic pain models, these compounds modulate TRPV1/A1 activation and normalize spinal cord synaptic plasticity. Recently we evaluated their potential visceral analgesic properties and showed that RvD2 and, to a lesser extent, RvD1 and RvE1 can reverse histamine-mediated sensitization of TRPV1 on dorsal root ganglion (DRG) neurons in vitro.

Aim : Here, we evaluated in vitro the effect of RvD2 on TRPV1 sensitization induced by supernatants of rectal biopsies collected from IBS patients. In addition, we evaluated the therapeutic effect of RvD2 in vivo using a mouse model of post-infectious VHS (PI-VHS).

Methods : First, DRG neurons were incubated overnight with IBS supernatants, before or after a 30-minute incubation with RvD2, in order to reverse or prevent TRPV1 sensitization, respectively. TRPV1 activation was assessed using Ca²⁺-live imaging and expressed as the increase in intracellular $\Delta[\text{Ca}^{2+}]$ (nM). Next, the effect of RvD2 was evaluated on VHS in a mouse model of PI-VHS. Briefly, Balb/C mice were infected with *C. rodentium* in the presence of ovalbumin (OVA). After clearance of the infection, mice were re-exposed to OVA leading to VHS. VHS was measured using the visceromotor response to colorectal distention. Hypersensitive mice were identified and then randomized to treatment with RvD2 or vehicle i.p. for one week, after which VHS was re-assessed.

Results : Overnight incubation with IBS supernatant resulted in sensitization of TRPV1, an effect that was significantly prevented (1078 ± 152 vs 453 ± 56 , $p < 0.0001$, Mann-Whitney test) and reversed (392 ± 56 vs 127 ± 23 , $p < 0.0001$, Mann-Whitney test) by incubation with RvD2. Of interest, these effects were abolished when DRGs were pre-incubated with O-1918, an antagonist of the RvD2 receptor GPR18. In vivo, the visceromotor response in 6 out of 7 mice was normalized by RvD2 while all mice ($n = 6$) treated with vehicle remained hypersensitive ($p = 0.035$, Mann-Whitney test).

Conclusions : Our findings demonstrate that a low dose of RvD2 significantly prevents and reverses IBS supernatant-induced sensitization of TRPV1 via interaction with its receptor GPR18. Furthermore, RvD2 normalized the visceral pain response evoked by colorectal distention in a preclinical model of VHS. Based on these data, we conclude that RvD2 or GPR18 agonists may represent interesting novel therapeutic compounds to treat IBS.

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DUODENAL HYPERPERMEABILITY AND EOSINOPHILIA AND SYMPTOMS IN FUNCTIONAL DYSPEPSIA PATIENTS ARE REDUCED BY PROTON PUMP INHIBITORS. L. Wauters (1), M. Lambaerts (2), D. Frings (2), A. Accarie (2), J. Toth (2), R. Farré (2), G. De Hertogh (3), J. Tack (1), T. Vanuytsel (1) / [1] UZ Leuven, Leuven, Belgium, Gastroenterology and Hepatology, [2] KU Leuven, Belgium, TARGID, [3] UZ Leuven, Leuven, Belgium, Pathology.

Introduction : We previously demonstrated increased duodenal mucosal permeability and low-grade inflammation with eosinophils in functional dyspepsia (FD) patients (Vanheel et al., Gut 2014). However, the role of acid suppression with proton pump inhibitors (PPI) in relation to these changes is unclear.

Aim : To study duodenal permeability, eosinophil infiltration and symptoms in healthy volunteers (HV) and FD patients before and after PPI.

Methods : Duodenal biopsies were obtained to study transepithelial electrical resistance (TEER) and paracellular passage of a fluorescein-labeled dextran (4kDa) in Ussing chambers and for histology. Eosinophils were counted on H&E-stained sections per high-power field (HPF; 0.24 mm²). High-sensitivity C-reactive protein (hs-CRP) was measured in blood. After the endoscopy, a naso-duodenal tube was positioned in the second part of the duodenum with aspiration of fluids before and after a liquid meal (Fortimel, 300kCal) with pH-measurement. Study procedures were repeated after treatment with pantoprazole 40mg OD for 4 weeks in healthy volunteers (HV) and FD patients. Participants filled out the Leuven Postprandial Distress Scale (LPDS) (Carbone et al., APT 2016) daily and Patient Assessment of Gastrointestinal Disorders Symptom Severity Index (PAGI-SYM) before and after PPI. Non-parametric and correlation analyses were performed within- and between-groups.

Results : In total, 24 HV (15 female, median (IQR) age 25.5 (24-32) years) and 10 FD (9 female, 28 (22-34) years) were included. Both fasting (6.0 (3.9-6.7) vs. 7.1 (6.6-7.3); $p < 0.001$) and fed (6.3 (5.6-6.5) vs. 6.6 (6.3-6.8); $p = 0.003$) duodenal pH increased after PPI in HV but not FD. Fasting and fed pH were similar between HV and FD both off- and on-PPI. TEER was similar with and without PPI in both HV and FD. There was no difference in TEER between HV and FD off- or on-PPI but dextran passage was significantly higher in FD vs. HV off-PPI (42.8 (21.7-90.4) vs. 19.2 (14.5-26.5) pmol; $p = 0.04$). Duodenal hyperpermeability in FD was normalized after PPI (42.8 (21.7-90.4) vs. 18.2 (10.6-24.2) pmol; $p = 0.03$) and a trend for increased passage in HV after PPI (19.2 (14.5-26.5) vs. 23.6 (13.9-36.4) pmol; $p = 0.05$) was found. Duodenal eosinophilia was present in FD vs. HV off-PPI (10.5 (8.3-18) vs. 3 (2-4) per HPF; $p < 0.0001$) and decreased after PPI (10.5 (8.3-18) vs. 4 (3-6) per HPF; $p = 0.03$) with no difference in hs-CRP within- or between-groups. Symptoms were present in FD compared to HV both off- and on-PPI (all $p < 0.0001$) with a trend for decreased scores in FD after PPI (LPDS 17 (8-19) vs. 6 (5-12) and PAGI 50 (27-62) vs. 38 (18-59); both $p = 0.06$). Correlation between TEER and dextran passage in HV off-PPI ($r = -0.69$, $p < 0.001$) was lost on-PPI ($r = -0.38$, $p = 0.06$). No correlation between permeability, eosinophil infiltration or symptoms and pH was found in HV or FD.

Conclusions : Duodenal hyperpermeability and eosinophilia as well as symptoms in FD at baseline are reduced by PPI. However, changes in barrier function and eosinophilia do not correlate with pH, pointing towards the involvement of other luminal factors which is the subject of ongoing research.

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CODEINE INDUCES MAJOR MOTILITY DISORDERS IN HEALTHY VOLUNTEERS: A RANDOMISED DOUBLE-BLIND PLACEBO-CONTROLLED CROSSOVER TRIAL. A. Geeraerts (1), H. Geysen (1), L. Ballet (1), C. Hofmans (1), T. Omari (2), A. Manolakis (1), N. Rommel (3), T. Vanuytsel (1), J. Tack (1), A. Pauwels (1) / [1] KU Leuven, Belgium, TARGID, [2] Flinders University, Australia, Department of Human Physiology, [3] KU Leuven, Belgium, ExpORL Department of Neuroscience, Deglutology.

Introduction : The adverse effects of short- and long-term opioid use, such as codeine and morphine, on the gastrointestinal tract are well known. More recently, studies showed that chronic use of opioids may induce oesophageal dysfunction with symptoms similar to achalasia (dysphagia) and a manometric pattern of functional oesophago-gastric junction outflow obstruction (OGJ-OO). However, little is known whether this is generalised or occurs only in susceptible subjects, and whether acute opioid administration has similar effects.

Aim : We aimed to investigate the effect of acute codeine intake on oesophageal motility in healthy volunteers (HV) in a randomised, double-blind, placebo-controlled, crossover trial.

Methods : Participants were tested during two visits, at least one week apart: one placebo (30mL glucose syrup) and one codeine (30mL of codeine phosphate 10mg/5mL) visit. During both visits, a High-Resolution impedance Manometry (HRiM, Unisensor, Attikon, Switzerland) catheter was placed transnasally. Thereafter, a feeding tube was placed transnasally to infuse codeine or placebo in the proximal stomach. Forty-five minutes post-infusion, the participants received different volumes (5mL and 20mL) of liquid and semi-solid boluses, classified as 0-4 according to the International Dysphagia Diet Standardisation Initiative (IDDSI) classification and bread boluses (2x2cm/4x4cm). HRiM analysis was performed adhering to the Chicago classification v3.0 using dedicated software (Solar GI, Laborie, Canada).

Results : Twenty-two HV (6 men, 36±3y) completed the study. Two participants were excluded from analysis: one due to colicky pain (rare side effect of codeine) and one because of the presence of an OGJ-OO during placebo. Median (IQR) values for the studied parameters are presented in Table 1. After codeine infusion, significantly higher values for integrated relaxation pressure 4 seconds (IRP4) were observed for all given boluses (liquid, semi-solid and bread). The distal contractile integral (DCI) was significantly increased after codeine intake only for the boluses of 5mL IDDSI0, 5mL IDDSI4 and for 20 mL IDDSI0. Furthermore, distal latency (DL) was significantly lower after administration of codeine in all conditions except for 20 mL IDDSI0 and 5 mL IDDSI3 (Table 1). Based on the Chicago Classification v3.0, acute administration of codeine induced a major oesophageal disorder in five HV (2 type III achalasia, 2 OGJ-OO, 1 distal oesophageal spasm) (p-value=0.047). Table 1: Median (interquartile range) values of IRP4, DCI and DL for codeine and placebo administration

	Placebo	Codeine	p-value
5mL IDDSI0 IRP4	8.3 (6.3 – 14.8)	15.5 (13.3 – 17.8)	<.0001*
5mL IDDSI0 DCI	1236 (548 – 1826)	1266 (913 – 3782)	0.014*
5mL IDDSI0 DL	7 (6.6 – 7.9)	5.9 (5.3 – 6.3)	0.009*
20mL IDDSI0 IRP4	8 (4.4 – 12.8)	13 (9.3 – 16.8)	0.017*
20mL IDDSI0 DCI	811 (627 – 1442)	1386 (1051 – 2133)	0.018*
5mL IDDSI1 IRP4	10.5 (7 – 18.3)	18.5 (10.5 – 25.3)	0.009*
5mL IDDSI1 DL	7.1 (6.4 – 10.3)	6 (4.9 – 6.6)	<.0001*
5mL IDDSI2 IRP4	9 (7 – 13)	18 (10.4 – 21.8)	0.014*
5mL IDDSI2 DL	7.6 (6.7 – 8.3)	6.5 (5.6 – 7.1)	0.008*
5mL IDDSI3 IRP4	9 (7 – 14.5)	18.5 (12.5 – 25)	0.005*
5mL IDDSI4 IRP4	11.5 (7 – 15.4)	20 (11 – 25.8)	0.005*
5mL IDDSI4 DCI	1010 (532 – 1611)	1386 (689 – 2291)	0.005*
5mL IDDSI4 DL	7.9 (7.1 – 8.5)	6.6 (6.1 – 7.3)	<.0001*
Bread2x2 IRP4	12 (10 – 16.5)	24 (14 – 29.5)	<.0001*
Bread2x2 DL	7.9 (7.6 – 8.5)	6.1 (5.6 – 6.8)	0.003*
Bread4x4 IRP4	13 (8.3 – 19)	18.5 (13.3 – 29)	0.0196*
Bread4x4 DL	9.8 (7.7 – 10.5)	7.2 (6.6 – 8)	0.004*

* survives stepdown Bonferroni correction
IRP4=integrated relaxation pressure; DCI=distal contractile integral; DL=distal latency; IDDSI=international dysphagia diet standardisation initiative

Conclusions : This study shows that acute administration of codeine increases OGJ resistance in HV and is able to induce major motility disorders such as achalasia and outflow obstruction in a subset of subjects. Further analysis is needed to explain the mechanism underlying this phenomenon.

- B17 -

IDENTIFICATION OF DETERMINANTS OF IRRITABLE BOWEL SYNDROME SYMPTOM SEVERITY IN PRIMARY CARE. C. Tack (1), K. Van Den Houde (1), F. Carbone (1), E. Colomier (1), E. Clevers (1), J. Arts (2), J. Tack (1) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Gastroenterology, [2] AZ Sint-Lucas Brugge, Assebroek/ Brugge, Belgium, Gastroenterology.

Introduction : Irritable Bowel Syndrome (IBS) is one of the most commonly seen functional gastrointestinal disorder in primary care. However, the characteristics of IBS at primary care level are largely unknown.

Aim : Our aims were to evaluate determinants of symptom severity in IBS patients, diagnosed by general practitioners in Belgium.

Methods : IBS patients, included by 43 general practitioners, filled out questionnaires evaluating demographics, Rome IV criteria, IBS subtype, IBS-symptom severity scale (IBS-SSS), anxiety (GAD), depression (PHQ9), somatization (PHQ15) and work productivity and activity impairment (WPAI). Data are shown as mean±SEM. Student t-test, uni- and multivariate correlation analysis, and Chi-square analysis was used to identify determinants of IBS-SSS. Patients were subdivided into severity categories based on IBS-SSS scores (normal: < 75; mild: [75; 175], moderate [175; 300], severe: ≥300).

Results : In 154 subjects (79% female, mean age 42±1.2 and mean BMI 23± 0.9) diagnosed with IBS by the general practitioner, the following stool pattern subtype distribution was found: 23, 25, 42 and 10% for constipation, diarrhea, mixed and normal respectively. Mean IBS-SSS according to subtype was 287±15, 266±15, 283±12, and 209±24 for constipation, diarrhea, mixed and normal respectively. IBS-SSS of the normal stool IBS subtype was significantly lower compared to other subtypes (p=0.008, p=0.05, p=0.009 to respectively constipation, diarrhea, and mixed). IBS-SSS was positively correlated with PHQ9 (R=0.41), PHQ15 (R=0.58) as well as GAD (R=0.34) with all p-values<0.0001. In multivariate analysis, only PHQ15 was a significant independent predictor of IBS-SSS (p<0.0001). 73 % of the IBS patients fulfilled the Rome IV criteria (Rome+). Rome+ patients showed significantly higher IBS-SSS scores compared to the Rome- group (299±8 vs. 202±16, p<0.0001). In Rome+ patients severe, moderate, mild, and normal IBS-SSS scores were present in respectively 49, 42, 8 and 1% patients compared to 21, 38, 31, 10% respectively for Rome- (p<0.0001). Somatization, depression ratings and anxiety scores were significantly higher in Rome+ compared to Rome- (mean PHQ15 12.9±0.5 vs. 9.5±0.7, p<0.001; mean PHQ9 7.2±0.5 vs. 5.3±0.8, p<0.05; mean GAD 7.5±0.5 vs. 5.3±0.7, p<0.05). In addition, the overall correlation of IBS-SSS and work productivity was 0.37 (p=0.0006) and 0.47 for impact on daily activities (p<0.0001). However Rome+ showed a higher correlation than Rome-, respectively 0.37 vs. 0.25 (NS) for work productivity and 0.49 vs. 0.42 (NS) for daily activities, indicating a larger negative impact of symptom severity on work productivity in Rome+.

Conclusions : In IBS diagnosed in primary care, symptom severity is related to anxiety, depression, and especially somatization, and the majority of patients fulfil the Rome IV criteria. Approximately one third do not fulfil Rome IV criteria and these have lower symptom severity and work productivity impact.

- B18 -

DOES MEASUREMENT OF SYMPTOMS DURING A GASTRIC EMPTYING TEST IMPROVE CORRELATION BETWEEN SYMPTOMS AND EMPTYING RATE? R. De Buysscher (1), K. Van Den Houde (2), J. Tack (2), F. Carbone (2) / [1] KUL, Belgium, TARGID, [2] Translational Research Center for Gastrointestinal Disorders (TARGID), KULeuven, Leuven, Belgium, Gastroenterology.

Introduction : Functional dyspepsia (FD) and idiopathic gastroparesis are both characterised by upper gastrointestinal symptoms such as epigastric pain, epigastric burning, postprandial fullness, bloating, early satiety, nausea, belching and a negative upper endoscopy. It has been debated whether it is necessary to distinguish these entities in clinical practice as previous studies showed a poor correlation between delayed gastric emptying (GE) and symptom pattern and severity. However, symptom questionnaires are usually based on recall of symptom burden over several weeks, whereas the GE test occurs at a single point in time.

Aim : The aim of the present analysis was to evaluate whether linking symptom assessment in time to the GE test allows a better symptom distinction between patients with normal and delayed GE.

Methods : We studied patients fulfilling Rome III FD criteria, referred for GE breath test using a ¹³C-octanoic acid labelled 250 Kcal meal. Frequency of symptoms was obtained by a symptom frequency questionnaire based on Rome III in the majority of patients. During the breath test FD patients scored the intensity of 6 symptoms (bloating, epigastric burning, nausea, pain, postprandial fullness and belching) on a 0-4 scale at 15 min intervals between 0 and 240 min. Meal-related severity of individual symptoms was obtained by summing all scores for the symptom (score:0 to 68). The sum of all symptom scores generates the global meal-related symptom severity. Patients were subdivided into normal and delayed GE rate (cut-off T1/2³ 109 min). Furthermore, the sum of bloating, nausea, pain and postprandial fullness scores were described as dyspepsia symptoms. Data are shown as mean±SEM. Data were analysed using non-parametric statistical tests, student t-tests, chi square tests and spearman correlation with p<0.05 considered statistically significant.

Results : A total of 504 FD patients (70% females, age 43.6±0.7 years, BMI 23.3±0.2 kg/m²) were recruited. Postprandial fullness and bloating were reported as the most severe symptoms (respectively, mean score 20±0.8 and 16±0.8), while nausea and epigastric burning were scored as least severe symptoms (mean score 12±0.7 and 10±0.7). Delayed GE was present in 122 patients (77% females, age 42.7±1.5 years, BMI 23.2±0.6 kg/m²) and normal GE was present in 382 patients (67% females, age 43.8±0.8 years, BMI 23.3±0.2 kg/m²). Patients with delayed GE reported higher postprandial fullness and bloating frequencies on the Rome questionnaire (at least 2 times a week) (respectively, 89% vs. 78%, p=0.03 and 86% vs. 75%, p=0.03). During the breath test global symptom severity tended to be higher in patients with delayed GE compared to normal GE (100±7.1 vs. 82±3.4, p=0.06). Patients with a delayed GE also showed a

tendency to more severe dyspepsia symptoms than patients with a normal GE (75 ± 5.9 vs. 59 ± 2.7 , $p=0.06$) and they had significantly higher meal-related scores for nausea (16 ± 1.6 vs. 11 ± 0.08 , $p=0.01$). Correlations between GE rate and the severity of symptoms for the total population (bloating: $r=0.05$, $p=0.2$; epigastric burning: $r=0.008$, $p=0.9$; nausea: $r=0.07$, $p=0.1$; pain: $r=0.009$, $p=0.8$; postprandial fullness: $r=0.05$, $p=0.3$ and belching: $r=-0.08$, $p=0.06$) and delayed GE patient population (bloating: $r=0.02$, $p=0.9$; epigastric burning: $r=-0.03$, $p=0.7$; nausea: $r=-0.04$, $p=0.6$; pain: $r=0.1$, $p=0.3$; postprandial fullness: $r=-0.04$, $p=0.7$ and belching: $r=-0.1$; $p=0.2$) were poor and not significant.

Conclusions : Even when symptoms are assessed during the test meal, symptom pattern is only minimally different between FD and idiopathic gastroparesis. There was a tendency to more severe dyspeptic symptoms but only nausea showed significantly higher meal-related scores for idiopathic gastroparesis compared to FD. Nevertheless, severity of symptoms was not associated to the severity of GE rate. These findings have important implications for the value of routinely applying GE testing in clinical practice.

- B19 -

FOOD ANTIGEN-SPECIFIC IGE-MEDIATED IMMUNE RESPONSE AS UNDERLYING MECHANISM LEADING TO VISCERAL HYPERSENSITIVITY IN IRRITABLE BOWEL SYNDROME (IBS). M. Florens (1), J. Aguilera-Lizarraga (2), E. Perna (2), S. Theofanous (2), R. Bisschops (2), A. Denadai-Souza (2), P. Jain (2), C. Breynaert (3), M. Wouters (2), G. Boeckxstaens (2) / [1] University Hospitals Leuven, Leuven, Belgium, TARGID, [2] University Hospitals Leuven, Belgium, TARGID, [3] University Hospitals Leuven, Belgium, Microbiology and Immunology.

Introduction : Ingestion of specific food products is commonly reported to trigger symptoms in IBS patients, however the mechanisms involved remain poorly characterized. We recently showed that mice develop an aberrant immune response to ovalbumin (OVA) during an intestinal infection, with development of mast-cell-mediated visceral hypersensitivity (VHS) upon re-exposure to OVA. Additionally, IBS patients demonstrated an immediate mucosal response upon rectal injection of food antigens, suggesting the involvement of a similar food antigen-specific mechanism leading to abdominal pain.

Aim : Here, we further evaluated the role of food antigen-specific antibodies in the development of VHS in mice and humans.

Methods : Balb/C mice were infected with *C. rodentium* in the presence of OVA. After clearance of the infection, mice were re-exposed to OVA or saline. VHS was assessed using the visceromotor response to colorectal distention. To eliminate B cells and plasma cells from the colon, mice were treated with a combination of an anti-CD20 antibody (5D2 clone) and bortezomib. To block the interaction between IgE and FcεRI and thereby prevent mast cell activation, mice were treated with an anti-IgE monoclonal antibody (R1E4 clone). In humans, to evaluate the potential role of IgE in IBS, quantitative immunofluorescence of IgE in rectal biopsies of HV and IBS patients was evaluated by confocal imaging.

Results : WT mice developed VHS upon re-exposure to ovalbumin (hypersensitive mice) but not to saline (normosensitive mice). In contrast, B- and plasma-cell-depleted mice or mice treated with a monoclonal antibody against IgE failed to develop VHS in response to ovalbumin re-exposure. Interestingly, increased ovalbumin-specific antibodies were detected in colonic tissue (but not in serum) of hypersensitive, compared to normosensitive mice. In humans, increased levels of IgE immunofluorescence on mast cells was detected in a subset of IBS patients, supporting our hypothesis that IgE-mediated mast cell activation is involved in IBS. Of interest, levels of IgE immunofluorescence positively correlated with abdominal pain severity in patients.

Conclusions : Our data support the concept that an intestinal infection can promote loss of oral tolerance to ovalbumin leading to IgE-dependent mast-cell-activation and VHS upon re-exposure to this food antigen in mice. Moreover, we provide evidence that a similar mechanism may be involved in IBS, potentially contributing to the induction of VHS by food ingestion.

- B20 -

RUMINATION SYNDROME AND SUPRA-GASTRIC BELCHING CAN BE DIAGNOSED BASED ON A 24 HOUR PH-IMPEDANCE MONITORING. H. Geysen (1), E. Clevers (2), T. Vanuytsel (2), J. Tack (2), A. Pauwels (2) / [1] KUL, Belgium, TARGID, [2] KU Leuven, Belgium, TARGID.

Introduction : Gastro-oesophageal reflux disease (GERD) is diagnosed by performing an upper endoscopy and/or a 24h pH-impedance (pH-MII) monitoring, the latter being the gold standard in reflux monitoring. Unfortunately, a 24h pH-MII monitoring cannot exclude the presence of rumination syndrome (RS) and supra-gastric belching (SGB), two important confounding entities, which are diagnosed by performing a high-resolution impedance manometry (HRiM) measurement with meal ingestion.

Aim : To examine whether a 24h pH-MII monitoring is able to discriminate between the different pathologies.

Methods : Patients with typical reflux symptoms undergoing a pH-MII monitoring and a HRiM with meal (University Hospital Leuven) within a period of one year were retrospectively analysed. Patients were classified into three subgroups

(reflux, SGB and RS) based on the HRiM measurement. Following pH-MII parameters were analysed: the number of reflux events, the number of reflux events with a high proximal extent (total, during 1st hour postprandial), oesophageal acid exposure time (AET), gas reflux (supra-gastric and gastric belching) and symptom association probability (SAP). Cut-offs were determined using a receiver-operating characteristic curve analysis.

Results : Forty-seven patients (19 male, 45y [33-56y]) were included (29 reflux, 11 SGB, 7 RS). The number of reflux events and number of reflux events with a high proximal extent on pH-MII were significantly higher in RS compared to reflux and SGB. The number of supra-gastric belches was significantly higher in SGB compared to other subgroups (Table 1). On average 20 symptoms were reported during the pH-MII monitoring in the reflux subgroup, 82 in SGB and 24 in RS ($p=0.0051$). Belching was more frequently reported in SGB compared to reflux and RS ($p=0.036$; $p=0.001$ resp.) and regurgitation was more frequently reported in RS compared to reflux ($p=0.0051$). RS patients more often displayed a positive SAP for typical symptoms compared to the reflux subgroup ($p=0.037$), there was a trend towards a higher number of RS patients with a positive SAP compared to SGB patients ($p=0.066$). A cut-off of 64 reflux events and 27 reflux events with a high proximal extent on pH-MII identified patients with RS with 85% sensitivity and 93% specificity. Reflux Supra-gastric belching Rumination syndrome p-value (main effect) Reflux events 31 (24-68)[a] 43 (14-72) 89 (64-266) 0.045 Reflux 1st hour pp 6 (4-9) [a] 3 (1-7) [b] 14 (10-26) 0.001 Bolus exposure 0.54 (0.31-1.13) 0.50 (0.08-1.02) 1.00 (0.78-2.35) 0.177 Proximal extent 7 (2-14) 8 (0-20) 44 (29-247) 0.007 Proximal extent 1st hour pp 1 (0-3) [a] 0 (0-2) [b] 10 (5-26) 0.001 Supra-gastric belching 0 (0-1) 74 (46-96) 0 (0-1) <0.0001 Gastric belching 8 (4-18) 3 (1-14) 7 (4-17) 0.176 AET 1 (0.30-3.80) 1.1 (0.06-8.2) 5 (0.43-9.80) 0.506 PPI=proton pump inhibitor;pp=postprandial;AET=acid exposure time [a]Post hoc analysis showed a higher number of reflux events [total ($p=0.03$) and during 1st hour postprandial ($p=0.01$)] and a higher number of reflux events with a high proximal extent [total ($p<0.001$) and during 1st hour postprandial ($p<0.001$)] in patients with rumination syndrome compared to the reflux subgroup. [b] Post hoc analysis showed a higher number of reflux events during 1st hour postprandial ($p=0.002$), a higher number of reflux events with a higher proximal extent [total ($p=0.038$) and during 1st hour postprandial ($p=0.002$) in patients with rumination syndrome compared to supra-gastric belching.

Conclusions : The total number of reflux events measured on pH-MII was significantly higher in patients with RS compared to the reflux and SGB subgroup. RS can be identified with good accuracy on 24h pH-MII, when using a cut-off of 64 reflux events and 27 reflux events with high proximal extent. SGB can be correctly diagnosed on pH-MII monitoring by focusing on the direction of gas flow events.

- B21 -

PROGNOSTIC PERSPECTIVES OF HYDROCHLORIC ACID ACIDINHIBITION EFFECTIVENESS EXPRESS DIAGNOSTICS IN STOMACH DURING HELICOBACTER PYLORI ERADICATION. I. Paliy (1), V. Chernobroviy (1), S. Zaika (1), I. Chernova (1), N. Kondratiuk (1) / [1] National Pirogov Memorial Medical University, Vinnytsya, Ukraine, Internal and Family Medicine.

Introduction : 24-hour gastro-pH-monitoring used to be the «golden standard» for control of PPI effectiveness. But because of its duration this method cannot be widely applied in everyday practice, which complicates control over PPI acid-blocking action effectiveness. As an alternative to 24-hour gastro-pH-monitoring, express-gastro-pH monitoring technique developed by prof. V. Chernobroviy (Ukraine) may be used. This technique allows analyzing the condition of secretory function in different anatomic-topographic sites of stomach during a short period of time.

Aim : To establish the criteria for pH values of express-gastro-pH monitoring for successful eradication H.p.

Methods : We analyzed the results of express-gastro-pH-monitoring in 49 patients with acid-dependent diseases of esophagus, stomach and duodenum infected with H.p. The patients were administered a triple eradication therapy in standard doses: PPI + clarithromycin + amoxicillin or ornidazole b.i.d. during 7 days. Acidoinhibition control was performed for all patients at $6,7 \pm 0,6$ day by express-gastro-pH monitoring. The control of eradication was carried out 4 weeks after eradication scheme completion. Acidoinhibition control was performed for all patients at $6,7 \pm 0,6$ day by express-gastro-pH monitoring. The control of eradication was carried out 4 weeks after eradication scheme completion. The analysis of express gastro-pH monitoring results was carried out by studying gastric pH: minimum pH (min pH), maximum pH (max pH), average arithmetic pH (X pH), mod pH (Mo pH), median pH (Me pH), as well as studying of correlation links by Spirmen's nonparametric method between minimum pH (min pH), maximum pH (max pH), average arithmetic pH (X pH), mod pH (Mo pH), median pH (Me pH), and H.p. eradication. According to the results of UBT, the patients were divided into groups: 39 patients with successful (group #1) and 10 patients with unsuccessful (group #2) eradication. The average age of group #1 was $41,7 \pm 2,7$ years, height $171,2 \pm 1,5$ cm, body weight $70,5 \pm 2,2$ kg. The average age of group #2 was $46,4 \pm 5,8$ years, height $169,6 \pm 2,1$ cm, body weight $68,8 \pm 2,6$ kg. The comparison did not reveal any likely differences between these groups ($p>0,05$).

Results : Comparison of express-gastro-pH monitoring parameters in the patients of both groups showed that group #2 patients had significantly lower ($p<0,05$) indices of intragastric pH compared to patients in group #1. In particular, min pH was ($3,6 \pm 0,45$ vs. $4,8 \pm 0,33$), max pH ($5,6 \pm 0,56$ vs. $6,8 \pm 0,16$), X pH ($4,2 \pm 0,61$ vs. $5,6 \pm 0,28$), Mo pH ($3,9 \pm 0,76$ vs. $5,7 \pm 0,3$) and Me pH ($4,0 \pm 0,55$ vs. $5,5 \pm 0,3$). A strong correlation ($p<0,03$) has been established between successful eradication and intragastric max pH ($r=0,3$) index during anti-helicobacter pharmacotherapy, as well as ($p<$

0,05) between successful eradication H.p. and average intragastric X-pH ($r=0,27$) index. Additionally, a correlation connection ($p < 0,03$) has been established between successful eradication H.p. and intragastric Mo pH ($r=0,3$) index. At the same time, for indices of min pH and Me pH such connection has not been established. Thus, for Spirmen ranges min pH index was 0,2 ($p > 0,05$), for Me pH $r = 0,25$ ($p > 0,05$).

Conclusions : When conducting H.p. eradication it is necessary that the indices of intragastric pH (according to the results of express-gastro-pH monitoring) were respectively for max pH $\geq 6,8 \pm 0,16$ un., for X pH $\geq 5,6 \pm 0,28$ un., for Mo pH $\geq 5,7 \pm 0,3$ un., since these indicators show a close correlation with successful H.p. eradication.

CASE REPORTS

- C01 -

A RARE COMPLICATION OF TRANSFISTULARY ENDOSCOPIC DRAINAGE AFTER SALVAGE ESOPHAGECTOMY FOR ESOPHAGEAL ADENOCARCINOMA. S. Ouazzani (1), J. Rigaux (2), I. Tancredi (3), E. Farinella (4), E. Toussaint (2) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, [2] CHU de Charleroi, Hôpital Marie Curie, Charleroi, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, [3] CHU de Charleroi, Hôpital Marie Curie, Charleroi, Belgium, Department of Radiology, [4] CHU de Charleroi, Hôpital Marie Curie, Charleroi, Belgium, Department of Digestive Surgery.

Postoperative morbidity and mortality rates occurring after surgery for esophageal cancer are high (34.7%, 8.4%). Anastomotic leakage is frequent after neoadjuvant radiochemotherapy (12.4%) and considerably increase postoperative mortality. Their treatment requires multidisciplinary approaches including endoscopic techniques with esophageal stenting or internal transfistulary drainage by double pig tail stents insertion. We report the case of a 77 years old man with locally advanced esophageal adenocarcinoma. A salvage transhiatal esophagectomy after chemoradiotherapy was performed. There was no complication in the immediate postoperative period and he was discharged from hospital at day 10. Twenty six days after surgery, the patient developed a severe sepsis. A CT scanner showed a postero-lateral left mediastinal collection next to the gastro-esophageal anastomosis, measuring 60x33x20mm. External drainage was not feasible due to its location (between aorta and left bronches). An upper gastrointestinal endoscopy was then performed showing an anastomotic leakage and a transfistulary drainage was done (by insertion of two short double pig tail stents). The treatment included intravenous antibiotics and artificial nutrition by nasojejunal feeding. The clinical response was good. Thirteen days later the patient developed severe hemoptysis. An angioscanner showed a pseudo-aneurysm of the left lower bronchial artery probably induced by the double pig tail stents. The pseudo-aneurysm was successfully treated by endovascular embolization, with resolution of hemorrhage, but the patient died due to ARDS. We reported a rare and serious complication of transfistulary endoscopic drainage. The use of this technique is increasing for the treatment of fistulas occurring after bariatric surgery and seems to be efficient and safe in this indication. In the setting of mediastinal collection, even more after radiochemotherapy, it appears that digestive endoscopists should be aware of the highest risk of complications.

- C02 -

CAPECITABINE: NOT ONLY HAND-FOOT SYNDROME. A. Van Oosterwyck (1), L. Bossuyt (2), M. Keuppens (3), S. Van Langendonck (1), M. Cool (1), G. Deboever (1), G. Lambrecht (1) / [1] AZ Damiaan, Oostende, Belgium, Gastroenterology, [2] AZ Damiaan, Oostende, Belgium, Dermatology, [3] AZ Damiaan, Oostende, Belgium, Pathology.

We present a 75-year-old man diagnosed with a pancreatic adenocarcinoma who underwent a Whipple procedure and was treated with gemcitabine-capecitabine post-surgery. Gemcitabine was started in a weekly scheme for three weeks with a one week break and capecitabine was administered daily and orally. After two weeks of treatment, he presented on our ward with a non-pruritic, non-blanching petechial rash on both lower legs and feet, despite having normal platelet counts. Our patient had no other complaints and he had not suffered from fever or infection. Clinically, a diagnosis of vasculitis was confirmed by our consulting dermatologist. The remainder of the clinical examination was unremarkable, with the exception of a red swollen toe due to a gout flare-up. Biochemically we found no abnormalities despite chemotherapy-induced grade 3 neutropenia for which reverse isolation was started. There was also some elevated CRP, most likely due to the gout. Autoimmune serology was negative, as well as urine sediment. We started empirically with one day of intravenous and then one week of oral corticosteroids with a positive response on the rash. Both capecitabine and gemcitabine were put on hold. A punch biopsy was obtained on the second day of admission (after the first administration of IV methylprednisolone) and showed a low grade vasculitis with eosinophils, but no leukocytic infiltration or fibrinoid necrosis. This can be classified as cutaneous small-vessel vasculitis. This so-called single-organ vasculitis can be caused by either systemic diseases, infection or neoplasm, but also by drugs. Given the exclusion of autoimmune disease, infection and given the relationship with the start of medication, it can be assumed that the culprit was indeed the chemotherapy. Treatment with corticosteroids remained successful and capecitabine was not reintroduced. There was a full resolution of the lesions. Gemcitabine was restarted as a trial and did not evoke a relapse. This led us to believe that capecitabine was the possible cause of the vasculitis. Discussion: The term vasculitis signifies the inflammation of a blood vessel, and there has to be made a difference between large-vessel, medium-vessel and small-vessel vasculitis. There are many possible etiologies. Important ones include autoimmune disease, infection, neoplasm and medication (1). It is therefore crucial to exclude systemic inflammation (2). Capecitabine, an oral prodrug of fluorouracil, is frequently used in the treatment of solid tumors, and its most well-known cutaneous side-effect is hand-foot syndrome. However a vasculitis-like rash following administration of capecitabine has been reported once

before in the medical literature (3). In this other case, pathology showed a leukocytoclastic vasculitis. They also found no systemic involvement and treatment consisted of prednisone. Vasculitis can range from urticarial vasculopathy to leukocytoclastic vasculitis with destruction and necrosis of the blood vessel wall. If extracutaneous disease is ruled out and the cutaneous small-vessel vasculitis seems to be triggered, therapy consists of removing this trigger as well as administration of supportive therapy (2).

Conclusion: In absence of systemic symptoms, drug-induced vasculitis should be considered in patients receiving capecitabine. It can manifest as a rare side effect of the drug, and can be treated effectively with a short course of oral corticosteroids. 1. Watts RA, Scott DG. Recent developments in the classification and assessment of vasculitis. *Best Pract Res Clin Rheumatol* 2009; 23:429-43. 2. Goeser MR, Laniosz V and Wetter DA, A Practical Approach to the Diagnosis, Evaluation, and Management of Cutaneous Small-Vessel Vasculitis, *American Journal of Clinical Dermatology*, 2014; 15, 4, 299-306 3. Al-Shamsi HO, Kee BK, Tetzlaff MT, et al. Capecitabine-induced leukocytoclastic vasculitis under neoadjuvant chemotherapy for locally advanced colorectal cancer. *J Gastrointest Oncol*. 2015;6(3): E40–E43

- C03 -

REDISCOVERING SURGICAL BILE DUCT EXPLORATION IN A MULTIMODAL APPROACH FOR COMMON BILE DUCT STONES (WITH VIDEO). L. Abreu De Carvalho (1), S. Van Cleven (2), O. Uyttebroek (2), P. Hindryckx (3), A. Vanlander (2), X. Rogiers (2), F. Berrevoet (2) / [1] Ghent University Hospital, Ghent, Belgium, HPB surgery, [2] Ghent University Hospital, Ghent, Belgium, Department of General and HPB surgery and liver transplantation, [3] Ghent University Hospital, Ghent, Belgium, Department of Gastroenterology.

Introduction : The treatment of gallstone disease has evolved since the upcoming of laparoscopic cholecystectomy (CCE). The subsequent exploration of the common bile duct (CBD) in case of CBD stones has not met an equal dissemination in the surgical community dominated by laparoscopy, maybe because of the high technicity required. In contrast, the endoscopic approach has become more common, but this does not provide an answer to all situations such as the growing population with a gastric bypass or allow a one-stage treatment when CCE is required.

Aim : Evaluate the results of our experience with a multimodal approach for CBD stones with endoscopic retrograde cholangiopancreatography (ERCP) and surgical bile duct exploration (BDE).

Methods : Since October 2016 a programme of surgical BDE has been implemented and the results were reviewed.

Results : In a 2-year period, 22 patients underwent a surgically assisted BDE. All cases were approached laparoscopically, with 2 cases of conversion to laparotomy. Three patients had a previous gastric bypass and 2 patients had a previous gastrectomy. A transgastric ERCP was performed in 2 cases. The other 20 patients underwent BDE, with transcystic approach in 16 cases (80%) and choledochotomy in 4 cases (20%). Preoperative diagnosis of acute cholecystitis with concomitant CBD stones in 7 patients, who were referred for an urgent laparoscopic CCE with BDE. In 2 patients, the perioperative incidental diagnosis of CBD stones was established by systematic cholangiography. Three patients underwent a BDE after a failed ERCP. Bile duct drainage was used in 2 patients and there were no cases of postoperative bile leakage. Overall success rate of BDE was 70% and most frequent reason of failure was an impacted stone at the duodenal papilla. In the 6 cases of failed clearance of the CBD, 2 intraoperative and 4 postoperative ERCP's were performed. In 18 patients (82%) there was a clearance of the CBD in a one-stage procedure.

Conclusions : Endoscopic and surgical approaches for gallstone disease with CBD stones are complementary and their combined application is safe and feasible. It allows a high rate of CBD clearance in a one-stage procedure.

- C04 -

HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS PRESENTING AS COMMON GASTROINTESTINAL SYNDROMES – THINK, ACT AND SEEK IMMUNOLOGICAL ALTERATIONS. S. Nullens (1), S. Naegels (1) / [1] ZNA Middelheim, Antwerpen, Belgium, Gastroenterology and Hepatology.

We present two cases of patients that were referred to the gastrointestinal department due to common gastrointestinal complaints, being anal blood loss and unexplained transaminase elevation. In a first case, a 21-year old male of Guinea presented to the Gastroenterology department with rectal bleeding. Earlier that month, the diagnosis of (presumed) amoebic dysentery was made for which he was treated with metronidazole and ceftriaxone. Rectosigmoidoscopy was compatible with ulcerative colitis, with pathology reports being more suggestive of an acute self-limiting infectious disease. No micro-organisms however could be identified except for the presence of *Schistosoma* eggs, for which praziquantel was started. Due to hemodynamic instability, the patient was transferred to the Intensive Care Unit. Because of therapy-unresponsive bleeding, a left hemicolectomy was performed, displaying extensive necrosis microscopically. After an initial recovery, rectal bleeding rapidly reoccured, as well as pancytopenia, transaminase elevation, hepatosplenomegaly and rising levels of lactate dehydrogenase and ferritin. The diagnosis of hemophagocytic lymphohistiocytosis (HLH) was made and the patient was treated with dexamethasone. Dosages however could not be tapered due to clinical

relapses, and rituximab as well as etoposide were added to the therapy. A serum PCR for Epstein-Barr virus (EBV) came back positive (> 100000 copies per mL), and serology testing showed an active hepatitis B with low viral titers (651 IU/mL) for which lamivudine was given. Despite aggressive supportive and causative care, the patient deteriorated and coagulopathy developed. He was transferred to a tertiary center, where he succumbed to his disease due to progressive multi-organ failure seven days later. The second case concerns a 51-year old woman that was admitted to the hospital due to type 1 respiratory insufficiency caused by *Pneumocystis jirovecii* pneumonia with interstitial lung disease. Infectious serology revealed the underlying presence of a high HIV viral load (>106 viral copies/mL) and low CD4 count (120/mL). Treatment with clindamycin and primaquine was initiated. After seven days, our ward was consulted for progressive transaminase elevation. Iron parameters were 'accidentally' ordered in the lab the same day. Upon review of the patient's records, it was noted that ferritin levels were extremely high (>10000 µg/L). Furthermore we measured a declining sodium, albumin, hemoglobin and platelets, as well as rising triglycerides levels. A diffuse rash developed. The likely diagnosis of an HLH was made, and the patient was transferred to the Intensive Care ward for initiation of dexamethasone, whereupon levels of ferritin and transaminases declined rapidly with full clinical recovery. The non-hereditary form of the hemophagocytic syndrome is a clinical entity presumably caused by abnormal immune activation resulting in tissue destruction. The underlying pathophysiology encompasses the inhibition of downregulation of immune cells such as macrophages and other lymphocytes. Inappropriate immune activation will result in excessive cytokine production, causing tissue damage. Pro- as well as anti-inflammatory cytokines are secreted, with the increased soluble IL-2 receptor (CD25) and IL-18 levels being more specific for HLH. Increased hemophagocytosis of red blood cells by macrophages in bone marrow or liver biopsies can be seen, but this is not a prerequisite for the diagnosis since only 5 out of 8 criteria (fever, splenomegaly, cytopenia, increased triglyceride levels and/or low fibrinogen levels, increased ferritin, high CD-25 levels, hemophagocytosis and/or low/absent natural killer cell activity) must be fulfilled. Pronounced immune (re)activation is a well known trigger in the development of HLH, the most common one being EBV. Case reports of the development of HLH after initiating HAART therapy in HIV have been published as well. Gastroenterologists can encounter patients with HLH when they are consulted for patients presenting with hepatitis and gastrointestinal bleeding due to developing coagulopathy. Key to swift diagnosis in the GI department are usually additional lab testing including iron parameters, upon which an extremely high ferritin can be seen (usually >10000 ng/mL with over 90% sensitivity and specificity for HLH) and elevated gamma-GT levels, representing the infiltration of immune cells in the biliary ducts. Prompt diagnosis of HLH is essential in order to immediately start life-saving therapy with corticosteroids and/or immune modulating therapy. Seeking the underlying cause is then the only thing that is left.

- C05 -

HEPATITIS B VIRUS REACTIVATION INDUCING SEVERE ACUTE HEPATITIS AFTER DIRECT-ACTING ANTIVIRAL THERAPY FOR CHRONIC HEPATITIS C VIRUS: A CASE REPORT. L. Schrooyen (1), I. Juriens (1), J. Rigaux (1) / [1] CHU de Charleroi, Hôpital Marie Curie, Charleroi, Belgium, Gastroenterology.

The chronic infection with either Hepatitis B Virus (HBV) or Hepatitis C Virus (HCV) is common in endemic areas but rare in developed countries. Usually, HBV replication is suppressed in case of co-infection by HCV. In vitro studies suggest a cytokine-mediated mechanism although the interaction between the 2 viruses remains poorly understood. The use of Direct-Acting Antiviral agents (DAA) inhibiting specifically HCV replication, related to more effectiveness and less adverse effects compared to previous pegylated interferon based regimens, tends to become the gold standard of HCV eradication. Recently, a growing number of case reports and several observational studies raise awareness on the reactivation of HBV during or after DAA therapy among HBV/HCV co-infected patients. We report the case of a 68-year old woman admitted in emergency department for upper abdominal pain since 3 weeks. Her medical past included arterial hypertension, gastroesophageal reflux and HCV/HBV co-infection without evidence of underlying cirrhosis (fibrotest 0.37 and fibroscan 4.8 kPa). She declared no use of hepatotoxic medications, neither alcohol. Her physical examination revealed jaundice and alteration in the mental status. Significant laboratory findings included mild inflammation (CRP 18 mg/L), acute kidney injury (KDIGO 4), severe cytolysis (ALT > 9 times normal upper limit), and hepatic dysfunction: mild thrombopenia, hyperbilirubinemia (total bilirubin 6.58 mg/dL), hypoalbuminemia and increased prothrombin time (INR 2.03). Further anamnesis revealed a recent 3 months DAA therapy with Sofosbuvir and Velpatasvir (Epclusa®) for chronic HCV infection (genotype 4). As shown by her serological status before treatment (HBsAg 103.5, anti-HBe -, anti-HBc +), she was an inactive carrier of chronic HBV infection, with a low pre-treatment HBV viral load (DNA 71 IU/ml). The next 2 months after the end of DAA therapy showed a sustained HCV clearance (RNA < 15 IU/ml) but an increased HBV replication (DNA > 1.0 billion IU/ml) without elevation of hepatic enzymes or hepatic dysfunction. Complementary biological tests ruled out other main causes of hepatitis, as other viral infections or auto-immune diseases. In contrast, HBV replication remained consistently high (DNA 0.8 billion IU/ml). Finally, a liver biopsy showed an inflammatory infiltrate of lymphoid cells contributing to piecemeal necrosis without any evidence of drug-induced hepatotoxicity. There were neither cirrhosis patterns. Overall, these findings suggested HBV reactivation with severe hepatitis and acute liver failure. A treatment with Tenofovir, a nucleotide analogue reverse-transcriptase inhibitor (NtRTI) was quickly initiated. Given the clinical course improvement, she was allowed to leave

the hospital under NtRTI drug regimen. Ambulatory follow-up at 1 month confirmed both hepatic tests and liver function improvement associated to a decreased HBV viral load (DNA 13500 IU/ml). HBV reactivation during or after HCV eradication with DAA therapy among HBV/HCV co-infected patients is a rising clinical situation requiring closer and extended monitoring. According to several observational studies, 24% of co-infected patients treated with DAA therapy will experience HBV reactivation and 9% will show clinical and/or biological signs of acute hepatitis. In contrast, liver failure is a rare complication and only a few clinical cases are reported. To our knowledge, this is the first case reported in Belgium. According to the American Association for the Study of Liver Diseases (AASLD), all patients initiating DAA therapy should be assessed for HBV co-infection with a complete serological status. A test for HBV DNA should be obtained prior to DAA therapy in patients who are HBsAg positive. Anti-HBV treatment should be started at the same time DAA therapy is initiated, for patients meeting criteria of active HBV infection. In contrast, patients with low or undetectable HBV DNA levels could be either receive prophylactic treatment for HBV for the duration of the DAA treatment or be monitored at regular intervals. Nevertheless, the use of specific anti-HBV drugs as NtRTI has not yet been studied in this particular context. There is still a lack of evidence about therapy modalities among patients with HBV reactivation. Further studies are needed to determine other risk factors, the best prophylactic drug regimen and its duration and follow-up modalities for co-infected patients treated with DAA therapy.

- C06 -

CONFUSION AFTER BARIATRIC SURGERY. C. Delbaen (1), M. Surmont (1), C. Salem (1), P. Eisendrath (1), M. Van Gossum (1) / [1] CHU Saint-Pierre, Brussels, Belgium, Gastro-Enterologie.

Introduction : Wernicke encephalopathy (WE) is an acute form of encephalopathy characterised by the classical triad of mental confusion, oculomotor dysfunction (ophthalmoplegia and nystagmus) and gait ataxia as a result of thiamine (vitamin B1) deficiency. It is mostly seen in patients with chronic alcohol abuse but can also appear in patients with poor nutritional status. On MRI findings of hyperintense signals (T2) in the dorsal medial thalamic nuclei, periaqueductal gray area and the third and the fourth ventricle are typical. The prevalence of WE in the general Western population, based upon the typical brain lesions observed at autopsy, is 0.4 to 2.8 percent, but can be as high as 12.5 percent in alcohol abusers.

Case presentation : A 43-year-old women with a history of drugs addiction, currently only using cannabis, and a gastric bypass Roux-en-Y two months ago resulting in a weight loss of 22kg was hospitalised. Since the surgery she suffered from abdominal pain and dysphagia for solid foods which was investigated one month before the hospitalisation with a gastroscopy, contrast radiography of the upper gastrointestinal tract and abdominal CT who were reassuring. Follow-up by a dietician revealed that she had a poor intake and was non-compliance regarding the prescribed nutritional supplements. She presented to the emergency department with worsening of her general condition and the emergence of vision problems, visual and auditive hallucinations and mental confusion. The neurological examination showed a mixed nystagmus, deficiency of the oculomotor nerve and cerebellar ataxia. The patient was somnolent and disorientated in time. Brain MRI showed hyperintense signal T2 Flair in both thalamic without restriction in the diffusion. She was started on high-dose intravenous thiamine (500mg, twice daily) in combination with other vitamins and minerals after which a quick recovery of her mental status was observed. She was discharged four weeks later for further neurological revalidation since ataxia and polyneuropathy persisted.

Clinical presentation : In this case the classical triad of WE was present but only one-third to half of the patients show it. There is a high incidence of mental status abnormalities (82%), but low incidence of oculomotor dysfunction (29%), gait ataxia (23%) and polyneuropathy (11%). Atypical clinical presentation includes stupor, coma, hypothermia, hypotension, vestibular dysfunction without hearing loss and beriberi heart disease. Aetiology and risk factors WE is the result of a deficiency of thiamine mostly seen in patients with chronic alcohol abuse but it's also described in patients with poor nutritional status caused by poor dietary intake, increased metabolic needs, malabsorption and increased loss. We described a case of non-alcoholic WE due to poor dietary intake and malabsorption after gastric bypass Roux-en-Y. More and more cases of WE are described in recent literature since the number of bariatric procedures is growing. A recent overview of Oudman, E. et al. (1) shows that there is no significant difference between the different bariatric surgery procedure (gastroplasty, Roux-en-Y gastric bypass and sleeve gastrectomy) regarding the latency between surgery and onset of WE. Symptoms usually occur 4 to 12 weeks after surgery. Risk factor for developing WE after bariatric surgery are vomiting, rapid weight loss, loss of appetite, alcohol abuse, postoperative infection, non-compliance with vitamins supplements and lost to follow-up.

Diagnose : WE remains a clinical diagnosis since thiamine blood level and imaging can be normal. Imaging studies can be helpful to rule out other diagnoses. Typical findings on MRI are hyperintense signals (T2) in the dorsal medial thalamic nuclei, periaqueductal gray area and the third and the fourth ventricle. MRI is more sensitive than CT, 53% and 13% respectively and has a sensitivity of 93%. **Conclusion**: Wernicke encephalopathy is a rare but severe complication after bariatric surgery; physicians should be attentive to, especially in patients with high risk and since the number of procedures is rising follow-up and preventive administration of vitamins and minerals is recommended. It's primarily a clinical diagnosis that can be confirmed by brain MRI, although not necessary for the diagnosis. Immediate treatment

with high doses thiamine is mandatory since belated treatment or untreated WE can lead to permanent neurological sequela and dead. IV infusion of glucose before thiamine administration can worsen symptoms. There is no consensus on the optimal dose or duration of treatment. (1) *Obes Surg.* 2018 Jul;28(7):2060-2068

- C07 -

ENDOSCOPIC MANAGEMENT OF A LARGE BLEEDING ESOPHAGEAL POLYP BY SUBMUCOSAL TUNNELING AND DISSECTION. Y. Mourabit (1), I. El Nakadi (2), L. Verset (3), P. Demetter (3), A. Lemmers (1), J. Devière (1) / [1] Erasme Hospital, Brussels, Belgium, Gastroenterology, [2] Erasme Hospital, Brussels, Belgium, Digestive Surgery, [3] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, Pathology.

Introduction : Large bleeding esophageal polyps represent a rare condition for which endoscopic management might be the key treatment.

Aims & Methods : We report a video illustrated case of an endoscopic submucosal tunneling and dissection (STD) of a large esophageal polyp.

Results : A 73 year-old man presented with dysphagia and recurrent upper gastrointestinal tract bleeding for the past year. Gastroscopy showed at 20cm of dental arches a 4cm long polyp with a large implantation foot (Paris 0-Is), ulcerated on the surface and bleeding at the slightest touch. Endoscopic ultrasound suspected a submucosal hypoechoic lesion classified uT2N0. Biopsies were inconclusive. CT of the mediastinum showed a significant narrowing of the lumen with no enhancement and no adenopathy in the mediastinum. Discreet 18 FDG uptake in the upper esophagus was shown by PET-CT. Patient was referred to our institution for medico-surgical management. Because of the incertitude of finding a cleavage plane between the lesion and the muscle layer, the procedure was started as a per oral endoscopic myotomy (POEM) approach, starting by an incision 2cm upstream of the oral side of the polyp and creating a tunnel under the lesion. With this approach, we could close the defect in case of muscular infiltration. Lifting of the submucosal space was achieved with injection of 20% glycerol and blue dye. Then mucosal incision and STD were initiated with an adjustable tip electrosurgical Knife and then switched to triangle tip knife (swift and spray coagulation modes). Once we confirmed a clean plane of cleavage between the lesion and the muscle and the possibility to dissect the submucosal space up to the anal side of the lesion, we ended the resection by opening the two lateral mucosal edges by classic ESD approach. Using the clip-traction method, the specimen was removed en-bloc after 180 minutes and prepared for pathology. Specimen size was 35x20 mm. Surprisingly there was no bleeding during the procedure and no nourishing large vessels in the submucosa. Finally, we injected 10mg of triamcinolone at the level of the resection edges and field, in prevention of secondary stenosis. Pathology excluded any malignancy and concluded to a fibro-vascular polyp. Clinical evolution of the patient was good, with no recurrence of bleeding and dysphagia at 6 months of the procedure.

Conclusion: Esophageal fibrovascular polyp is a rare benign etiology of dysphagia and recurrent upper gastrointestinal bleeding. Typical endoscopic features of such lesion are highlighted in this video. Tunneling approach permitted to insure resectability with a possibility of changing our approach by closing the tunnel opening in case of muscular infiltration. A potential advantage of this approach might be lower per procedural bleeding by dissecting under this vascular lesion.

- C08 -

A LIVER ABSCESS FROM INDIA. C. De Herdt (1), S. Bourgeois (2) / [1] University of Antwerp, Antwerp, Belgium, internal medicine, [2] ZNA Stuivenberg, Borgerhout, Belgium, Gastroenterology.

Liver abscesses are classified into three categories; infectious, malignant and iatrogenic. Infection due to the protozoan, *Entamoeba histolytica*, can result in amebic colitis as well as an amebic liver abscess. *E. histolytica* belongs to the top three deadly parasites worldwide. Areas with high rates of amebic infection include India, Africa and Mexico. Compared with other parasites, the life cycle of *E. histolytica* is relatively simple and consists of two stages: the infectious cyst and the disease-inducing trophozoite stage. Humans are the primary known reservoir. Initial infection occurs after ingestion of faecally contaminated water or food containing *E. histolytica* mature cysts. A forty one-year old man presented at the emergency because of a sharp pain at the right hypochonder since two days. No fever was measured. The patient has been at home for five months after a six-week trip to India. Clinical examination revealed a deep pressure pain at the right hypochonder. Blood results showed a mild elevated CRP. After giving pain medication, the patient was send home and had to present himself to the department gastro-enterology the day after. An echography of the liver showed no abnormalities. The diagnosis of postinfectious irritable bowel syndrome was made. One day later he presented himself at another emergency because of no improvement of the abdominal pain. Clinical examination of the abdomen revealed a diffuse superficial pressure pain. Biochemically CRP was further elevated. CT scan of the abdomen was performed which showed a hypodens lesion at the right liver lob with an oedematous outer rim, suspected for an amebic liver abscess. The patient was admitted at the department of gastro-enterology. Initial treatment consisted of ciprofloxacin and metronidazole. A CT-guided puncture of the liver abscess was organized. Two milliliters of pus was evacuated

and send for culture and PCR for *E. histolytica*. Hemocultures and culture of pus remained negative. Serology for *E. histolytica* was positive five days after admission. Ciprofloxacin was discontinued. Patient received metronidazole for ten days, followed by seven days paromomycin. Two weeks after admission diagnosis of amoebic liver abscess was confirmed by positive PCR for *E. histolytica* on pus. The diagnosis of amoebic liver abscess relies on liver imaging and positive amoebic serology. Diagnostic fluid aspiration from the lesion is not necessary. Serology has a high sensitivity and specificity, but can be false negative the seven first days of infection. PCR for *E. histolytica* on liver pus or stools has an equivalent sensitivity and specificity as serology. However PCR has some disadvantages, the test is not available worldwide, is expensive and results are not immediately available. CT scan of the abdomen is preferred to exclude associated intra-abdominal infection. Most important differential diagnosis consist of pyogenic liver abscess, which is much more prevalent in the western world. Once considered a fatal infection, amoebic liver abscess is now considered a very treatable condition. Treatment entails the use of metronidazole. Since it is impossible to differentiate between an amoebic and pyogenic liver abscess on imaging, both have to be treated until serology for *E. histolytica* is positive. So initial treatment consists of metronidazole and a broad spectrum of antibiotic such as piperacilline-tazobactam, ceftriaxone or ciprofloxacin. Although there is an increasing resistance to ciprofloxacin for *E. coli* and *K. pneumoniae*. As parasites can persist in the intestine after administration of metronidazole, treatment should be followed by a luminal agent such as paromomycin. Drainage of the liver abscess is not indicated for all amoebic liver abscesses.

- C09 -

GANGLIONIC TUBERCULOSIS IN A CROHN'S DISEASE PATIENT TREATED BY INFLIXIMAB DESPITE ANTI-TUBERCULOSIS CHEMOPROPHYLAXIS. S. Vieujean (1), T. Bury (2), L. Gaspard (3), J. Giot (3), S. Maweja (4), E. Louis (1), C. Van Kemseke (1) / [1] CHU Liege, Liège, Belgium, Department of Gastroenterology, [2] CHU Liege, Liège, Belgium, Department of Pneumology and Allergy, [3] CHU Liege, Liège, Belgium, Department of infectious disease, [4] CHU Liege, Liège, Belgium, Department of abdominal surgery.

Infliximab is an IgG1 κ monoclonal antibody against tumor necrosis factor- α (anti-TNF α) who have significantly improved the management of patients with Inflammatory Bowel Diseases (IBD), but with an increased risk of opportunistic infection, especially tuberculosis (TB). We report a case of a 54 years-old man with an ileal Crohn's disease (CD) diagnosed in July 2014 (Montreal classification at diagnosed: A2L1B1p-). Patient was an active smoker and was treated by budesonide for several flares. Two years after diagnosis, since he has been hospitalised for subocclusion treated with methylprednisolone, combination therapy by mercaptopurine and anti-TNF α was discussed for steroid dependence. Patient was screened for tuberculosis (TB). A latent tuberculosis (LTB) was highlighted based on a positive interferon-gamma release assay (QuantiFERON TB) without clinical, microbiological and radiological evidence of active disease. A nine-month course of isoniazid (INH) 300 mg/day was started 4 weeks before the combination therapy with thiopurine/infliximab at the recommended doses. This treatment allowed a clinical remission and thiopurine could be stopped. Six months after completing INH for LTB and 1 month after cessation of thiopurine, patient was admitted in our emergency department for fever, dyspnoea and cough. Chest tomography showed large lymphadenopathies in the right pulmonary hilum and in the mediastinum. A fibroscopy with a bronchoalveolar lavage (with looking for bacillus of Koch) and an endobronchial ultrasound with biopsies were performed, both negative. Finally, a diagnosis of ganglionic tuberculosis was settled by a positive microscopic exam (auramine coloration) on an excised cervical lymphadenopathy. No resistance to usual anti-tuberculosis treatment was highlighted. Infliximab was immediately discontinued and anti-tuberculosis 4-drug regimen was initiated. Patient received Vedolizumab as IBD treatment 1 month later and he did not present any recurrence of TB infection or new flare of Crohn's disease up until now. This case report emphasizes that chemoprophylaxis for LTB does not completely protect against reactivation of TB in IBD patients treated by anti-TNF. It could be useful to study risk factors for reactivation of LTB in this treated by biologics population (monotherapy or combination therapy) to establish a case-by-case monitoring.

- C10 -

BILIARY PAPILLOMATOSIS. M. Struyve (1), F. Gelders (2), D. Geusens (3), S. van der Merwe (4) / [1] Ziekenhuis Oost Limburg (ZOL), Genk, Belgium, Gastroenterology, Hepatology and Endoscopy, [2] University Hospital Gasthuisberg, Leuven, Belgium, Internal Medicine, [3] University Hospital, Gasthuisberg, Leuven, Belgium, Gastroenterology and Hepatology, [4] University Hospital, Gasthuisberg, Leuven, Belgium, Gastroenterology, Hepatology and Endoscopy.

Introduction : We report here clear radiologic, endoscopic, cholangioscopic and histopathologic images and video of biliary papillomatosis. Aim: The aim of this abstract is to illustrate a case of biliary papillomatosis illustrated with the aid of clear radiologic, endoscopic, cholangioscopic and histopathological images and video.

Case report : A 74-year-old asymptomatic man was referred to the outpatient clinic by his general practitioner because of abnormal liver enzymes. He had no important medical history. Blood analysis showed mild cholestasis. Abdominal

computed tomography showed bile duct dilatation with contrast capturing mural nodules in the common bile duct with protrusion into the dilated lumen (Figure 1). Magnetic resonance cholangiopancreatography revealed bile duct dilatation with multiple irregular filling defects (Figure 2). We performed an endoscopic retrograde cholangiography that disclosed diffusely dilated bile ducts with a ragged appearance of the bile duct wall with multiple convex gaps as a sign of intrinsic compression (Figure 3). Single operator cholangioscopy was performed at the same time with direct visualization of numerous papillary mucosal projections wide spread in the common bile duct with nearly obliteration of the lumen of the bile duct (Figure 4 and Video). Targeted biopsies were taken of these intraductal lesions. The diagnosis of biliary papillomatosis was made and histologically proven (Figure 5). Biliary papillomatosis is a rare premalignant condition arising from the peribiliary progenitor cells. We report clear radiologic, endoscopic, cholangioscopic and histopathologic images and video of biliary papillomatosis.

- C11 -

A BILIARY CAST SYNDROME MIMICKING INTRAHEPATIC CHOLANGIOCARCINOMA. W. Soub Defeu (1), M. El Koulali (2), M. Ibrahim (2), N. Boon (2), T. Gustot (2), C. Moreno (2), D. Degré (2), M. Pezzullo (3), V. Lucidi (4), O. Le Moine (2), J. Devière (2), A. Lemmers (2) / [1] C.U.B. Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium, Gastroenterology, Hepatopancreatology and Digestive Oncology. [2] C.U.B. Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium, Gastroenterology, Hepatopancreatology and Digestive Oncology. [3] C.U.B. Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium, Radiology, [4] C.U.B. Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium, Abdominal Surgery.

Biliary cast syndrome (BCS) is an uncommon complication described in orthotopic liver transplant recipient characterized by molded intrabiliary black material and secondary biliary obstruction. Cholangiographic features of BCS are poorly known by endoscopists and hepatologists. We describe here a particular presentation of BCS in which the follow-up gave the diagnosis.

We report a case of a BCS and its endoscopic management. A 56-year-old male with a history of hypertension and liver transplantation for hepatocarcinoma with cirrhosis of mixed origin (Hepatitis C and alcohol) 10 years ago, presented with cholestasis associated to a 34 x 40 mm lesion suspended in the VIII biliary segment. An ERCP allowed to extract lithiasis fragments after biliary sphincterotomy and to brush segment VIII for cytology sampling, which was negative for cholangiocarcinoma. An EUS with FNA disclosed inflammatory tissue with no neoplastic cells. Knowing the negative balance and the general condition of the patient, decision was made to follow the patient by MRCP. A discrete increase of the segment VIII lesion size and changes in its features led to the decision to perform a cholangioscopy at 6 months to obtain histological evidence before possible surgical treatment. The cholangioscopic picture was in favour of intrahepatic biliary neoplasia (villous aspect of the mucosa) with upstream intrahepatic black stone. Several biopsies done under direct visualization were performed and showed chronic cholangiopathy with no sign of associated malignancy. Due to all the previous negative results and the good condition of the patient, the decision was taken not to resect the lesion and to follow him by MRCP every six months. After 2 years, he developed a septic cholangitis episode and increased cholestasis. MRCP showed necrotic saccular dilatation of the right intrahepatic bile duct at the former segment VIII lesion site, associated with distal migration of material at the choledoco-choledochal anastomosis. By ERCP, we obtained complete removal of the material which was compatible with cast in two sessions, with temporary plastic stents placement to ensure optimal biliary drainage in between. The evolution of the patient was rapidly favorable both clinically and biologically. At one month of follow-up, there was no recurrence of cholangitis nor cholestasis.

This case illustrates a rare presentation of tardive intrahepatic BCS initially mimicking an intrahepatic cholangiocarcinoma ten years after liver transplantation. The follow-up of the patient gave the clue, and highlights ERCP management of BCS.

- C12 -

IDENTIFICATION OF A NEW HEPATOCYTE NUCLEAR FACTOR 1ALPHA MUTATION IN A PATIENT WITH LIVER ADENOMATOSIS AND MODY 3. M. Surmont (1), C. Salem (2), C. Delbaen (3), V. Lucidi (4), J. Mulkay (2), T. Sersté (2) / [1] CHU Saint-Pierre, Brussels, Belgium, hepato-gastroenterologie, [2] CHU Saint-Pierre, Brussels, Belgium, hepato-gastroenterologie, [3] CHU Saint-Pierre, Brussels, Belgium, hepato-gastroenterologie, [4] Erasme Hospital, Brussels, Belgium, Liver transplant unit.

Background : Maturity-Onset Diabetes of the Young type 3 (MODY 3) is caused by several heterozygous germline mutations in the Hepatocyte Nuclear Factor 1alpha (HNF 1A) gene. The inactivation of this specific gene has been identified in a subgroup of hepatocellular adenomas: the so-called HNF 1A-mutated hepatocellular adenomas (HCA). The clinical entity characterized by ten or more hepatocellular adenomas is called liver adenomatosis. It is especially rare to identify liver adenomatosis in individuals with MODY 3. In these patients, the genetic testing is particularly interesting.

Case presentation : We describe the case of a genetically-proven HNF 1A mutation occurring in a young woman suffering from MODY 3 and liver adenomatosis. She was diagnosed with early-onset non-insulin-dependent diabetes mellitus at the age of seven. Two of her three brothers were diabetic as well. Genetic evaluation was performed at the age of nineteen: testing on blood sample revealed a heterozygous germline mutation of HNF 1A, c.827C>A (p.Ala276Asp) in exon 4, and the diagnosis of MODY 3 was established. Subsequently, the patient was lost to follow-up in her referential centre. At the age of 27 (and four months post-partum), she was admitted to the hospital for abdominal pain located at the right upper quadrant without fever. She had a history of oral contraceptive use and was now treated with subcutaneous insulin. Clinical examination showed no abnormalities. Laboratory testing didn't disclose abnormalities. Computed tomography revealed a homogenous liver parenchyma with numerous masses of different sizes. Retrospectively, multiple small lesions were seen on computed tomography five years before. Magnetic resonance imaging showed numerous (> ten) fat-containing nodules disseminated in the liver parenchyma. The largest lesion was situated in segment V, had a size of 64 x 44 mm with a heterogeneous aspect and had a marked hypervascular component. The use of a hepatobiliary contrast agent (Primovist®) didn't disclose hypercaptation of the lesions. The diagnosis of steatotic adenomatosis of the liver and H HCA was highly suspected. Percutaneous biopsy of the dominant liver lesion showed benign hepatocellular proliferation without evidence of bile ducts in the tumor; this was consistent with steatotic adenoma of the liver. Because of the volume of the largest lesion and the symptomatic disease, bisegmentectomy V-VI was performed. Postoperative excisional macro-biopsies showed typical steatotic adenomas without dysplasia. Genetic analysis of the DNA extraction from this adenoma revealed a c.827C>A heterozygous mutation in exon 4 (mean coverage >1000, in 52.1% of the analysis). This mutation was identical to the HNF 1A germline mutation, previously identified. The mutation c.827C>A of the HNF 1A gene has been described in MODY 3 in recent literature but has never been identified in H HCA.

Conclusions: The association between HNF 1A mutation and H HCA is well described. In this exceptional case, a young woman previously known with a c.827C>A (p.Ala276Asp) mutation of HNF 1A and suffering from MODY 3 was admitted with a symptomatic liver adenomatosis. Genetic analysis of the DNA extracted from the largest adenoma confirmed the same HNF 1A mutation. This clinical case is particularly interesting: first, because it highlights a specific mutation in HNF 1A, previously described in MODY 3 but never identified in liver adenomatosis. Second, this case underlines the importance of surveillance of liver adenomatosis in MODY 3 patients aiming to prevent life threatening complications, such as haemorrhage and malignant transformation. Currently, screening and follow-up of H HCA are not included in guidelines for the management of MODY 3 patients.

BELGIAN SOCIETY FOR GASTROINTESTINAL ENDOSCOPY (BSGIE)

- G01 -

COLORECTAL POLYPECTOMY, ARE WE MOVING IN THE RIGHT DIRECTION? BELGIAN SPECIFIC SUB-ANALYSIS OF AN INTERNATIONAL STUDY. J. Geldof (1), D. De Looze (2), L. Desomer (3), D. Tate (2) / [1] UZ Gent, Gent, Belgium, Maag-, Darm- en Leverziekten, [2] UZGent, Gent, Belgium, Maag-, Darm- en Leverziekten, [3] AZ Delta, Belgium, Maag-, Darm- en Leverziekten.

Introduction : Colonoscopy and polypectomy reduce the incidence and mortality of colorectal carcinoma (CRC). Basic polypectomy and understanding the principles of advanced polypectomy are considered fundamental skills for every endoscopist. Despite this polypectomy is commonly incomplete (CARE study 2013, Pohl) and international practice is heterogenous. In particular, data regarding Belgian polypectomy practice is scarce.

Aim : We aimed to compare the current polypectomy practice of Belgian colonoscopists with the standards set out in the ESGE colorectal polypectomy guideline (2017).

Methods : The study is a subgroup analysis of a larger international study of polypectomy involving 7 Western countries (Australia, Belgium, Canada, Israel, New Zealand, the UK and the USA). An online survey addressed to active endoscopists (identified via national gastroenterological and surgical societies) was developed. It contained questions regarding participant demographics, specific polyp images and the techniques the participant would apply to resect them in their daily practice. The survey was sent out by email to all members of participating societies in May 2017. A reminder was sent a few weeks later and the survey was closed in August 2017. Survey responses were compared with the ESGE colorectal polypectomy guideline of 2017.

Results : 664 Belgian endoscopists received the survey as member of either VVGE – Vlaamse Vereniging voor Gastro-Enterologie (Flemish Association of Gastroenterology), SRBE – Société Royal Belge de Gastro-Entérologie or BSGIE – Belgian Society of Gastrointestinal Endoscopy. 102 (15,4%) practitioners completed the survey. Of them 29 (28,4%) were trainees and 22 (21,6%) were considered tertiary endoscopists at the time of inquiry. Concerning the questions on polyp resection technique for depicted lesions, 17 (16,7%) respondents correctly identified management for both small lesions (3mm and 8mm ascending colon polyps). Only 17 (16,7%) chose cold snare polypectomy as preferred resection technique for the 8mm lesion. 70 (68,6%) respondents answered correctly on questions how to resect two intermediate size polyps (10mm and 15mm). 55 (53,9%) participants correctly identified management for all large lesions (20mm polyp in ascending colon, 45mm polyp in ascending colon, 45mm polyp in rectum). When shown a picture of an 80mm lesion with an endoscopically evident submucosal invasive component in the rectum, 9,8% of responding endoscopists chose to try endoscopic resection instead of referring for surgical treatment. Endoscopists with more than 10 years of experience were more likely to suggest correct management for the 3mm (82,7% vs 61,5% p=0,027) and the 15mm polyp (89,2% vs 69,4% p=0,013). Respondents who perform more than 10 colonoscopies per week were also more likely to suggest correct treatment for the 15mm polyp (92% vs 53,8%, p<0,001). No other significant differences could be found comparing subgroups of respondents. Regarding polypectomy technique preferences 65,7% routinely use CO2 insufflation, 63% use digital visualization enhancement techniques and 6,9% routinely use chromoendoscopy. Strikingly, for cold snare polypectomy and for EMR respectively 1/3 and 1/5 of all participants could not answer the question as to what type of snare they routinely use.

Conclusions : Adherence to the ESGE colorectal polypectomy guideline of 2017 amongst Belgian endoscopists is good regarding the resection of intermediate and large colorectal lesions. For smaller lesions there seems to be room for improvement, particularly regarding the low utilisation of cold snare polypectomy, especially in endoscopists with less experience. This observation could be a stimulant to develop a competency based education program in basic polypectomy techniques for GI trainees on a national level.

- G02 -

COLD SNARE POLYPECTOMY FOR LARGE NON-PEDUNCULATED POLYPS. A SERIES OF 129 POLYPECTOMIES. L. Van Overbeke (1), M. Ferrante (2), L. Mortier (2), J. van Dongen (2), G. Mertens (2), S. Ilegems (2) / [1] AZ Sint Maarten, Mechelen, Belgium, gastroenterology/*hepatology, [2] AZ Sint Maarten, Mechelen, Belgium, gastroenterology.

Introduction : Cold snare polypectomy (CSP) is an accepted technique to remove diminutive or small (6-9 mm) polyps. Here we present a series of CSP for advanced non-pedunculated polyps (> 10 mm).

Aim : To assess the efficacy and safety of cold snare resection for large non-pedunculated polyps.

Methods : This is a retrospective, single operator study. A total of 111 patients with non-pedunculated polyps (Paris classification 0-IIa, 0-IIb, 0-Is) estimated > 10 mm, underwent CSP.

Results : A total of 129 polyps were removed (87 0-IIa, 18 0-IIb, 24 0-Is). The number of these polyps ranked according to size was as follows: 11-19 mm: 63 (49%), 20-29 mm: 44 (34%), > 30 mm: 22 (17%). Thirty-eight (29.5%) were

sessile serrated adenomas, 47 (36%) were tubular adenomas, 25 (19.3%) were villous adenomas and 18 (14%) were hyperplastic polyps. Forty-nine (38%) polyps were resected in a piecemeal fashion, submucosal injection with diluted Indigo Carmine was used in 24 (19%). Immediate oozing bleeding was frequent but in almost all patients rapid spontaneous haemostasis occurred. In only one patient haemostatic clipping was required (in order to achieve haemostasis). Preventive clipping was used in 3 patients. There were no complications. Seventy patients had a follow-up colonoscopy. Of these 70 patients 9 had residual adenomatous tissue (12.8 %). According to the size of the original polyp, the numbers were as follows: 11-19 mm: 2/26 (7.7 %), 20-29 mm: 4/22 (18.2 %), > 30 mm: 3/13 (23%). Two of these patients were referred for surgery; one because of involvement of the appendiceal orificium, the other because of a difficult localization on the ileocaecal valve and presence of carcinoma in situ. The others patients underwent further cold resection; of those two had a negative follow-up (the others are scheduled).

Conclusions : CSP for advanced, non-pedunculated lesions is feasible and effective. The rate of residual adenomatous tissue could be further lowered by resecting an additional rim of normal tissue (as a surrogate for thermal ablation of the post-EMR margin). Most important CSP was completely safe in these series: there were no complications. Because of the increasing number of screening colonoscopies we are confronted with huge numbers of polypectomies. Safety is an extremely important issue because only a minority of the polyps would develop into colon cancer and ultimately the goal of colon cancer screening is to increase the chance of a healthy life and not to remove polyps per se. A polypectomy should therefore be effective and safe which was the case in these series of CSP.

- G03 -

ENDOSCOPIC OVERESTIMATION OF POLYP SIZE LEADS TO INCORRECT SURVEILLANCE INTERVAL.

A. Billiet (1), A. Vanden Bulcke (2), S. Van Langendonck (3), K. Hertveldt (4), M. Cool (3), G. Lambrecht (3), G. Deboever (3) / [1] University Hospitals Leuven, Leuven, Belgium, Internal medicine, [2] UZ Leuven, Leuven, Belgium, Gastroenterology, [3] AZ Damiaan, Oostende, Belgium, Gastroenterology, [4] AZ Damiaan, Oostende, Belgium, Pathology.

Introduction : Current colorectal cancer guidelines recommend more frequent colonoscopic surveillance in patients with large polyps (>1cm). In practice, polyp size is often based on endoscopic estimation.

Aim : The aim of this study was to investigate the accuracy of size estimation during colonoscopy and define the impact on subsequent clinicians' recommendation of surveillance interval.

Methods : A monocentric, prospective study was performed between April and October 2018. Colonoscopists determined polyp size by visual estimation without support of a biopsy forceps or other devices. Endoscopic size estimation was compared with ex-vivo prefixation and postfixation measurements. Ex-vivo prefixation measurement was considered the gold standard. Hyperplastic polyps and diminutive polyps (<5mm endoscopic estimation) were excluded, as these were often discarded. Furthermore, polyps were excluded if they were not removed in their integrality or had undergone piecemeal resection. To address the possible effect of fixation we calculated average decrease in size between ex-vivo prefixation and postfixation measurements. Other factors that influence surveillance interval (villous histology, high grade dysplasia, number of polyps) were collected from patient records and pathology reports.

Results : After exclusion of 14 polyps, a total of 100 polyps from 87 patients were included. The average age was 66.9 (± 11.8) years and 56.3% were men. Our study group comprises 72% (72/100) pedunculated and 28% (28/100) sessile polyps. Average decrease in size between ex-vivo prefixation and postfixation measurements was 2.7%. Endoscopic overestimation of polyp size was seen in 59% (59/100) of cases and was more frequent than underestimation (22% - 22/100). The degree of overestimation tended to decrease as the study progressed albeit non-significantly; 68% (17/25) of the first 25 polyps were overestimated versus 56% (42/75) of the remaining ($p=0.35$). An inappropriate surveillance interval was recommended in 20.0% (20/100) due to endoscopic overestimation. After considering other factors that define advanced polyps, 12% (12/100) still received an inappropriate surveillance recommendation.

Conclusions : Endoscopic determination of polyp size is prone to overestimation resulting in inappropriate surveillance recommendations. This may lead to increased costs and patient risk due to unnecessary colonoscopy. Formalin fixation did not significantly influence polyp size. It was remarkable that overestimation tended to decrease as the study progressed, possibly owing to an awareness effect. We suggest that endoscopic size estimation could improve with increased awareness by training, experience or confrontation with ex vivo measurements, but this should be tested in clinical trials. New tools such as linear probes and grid visual cues could help to improve the accuracy of endoscopic estimation. Further research is needed to assess whether these new endoscopic tools can replace ex vivo measurements to determine surveillance intervals. Until then ex vivo measurements should be used to establish surveillance intervals.

- G04 -

CAPNOGRAPHY DURING DAY TO DAY ENDOSCOPY – A VALUE-BASED HEALTHCARE PILOT IN A HIGH-VOLUME GASTROENTEROLOGY PRACTICE. R. Bisschops (1), I. Demedts (1), P. Roelandt (1), C. Doods (2),

I. Hoffman (3), R. Weissbrod (4), R. Saunders (5), M. Hiele (1), G. Van Assche (1) / [1] University Hospitals Leuven, Belgium, Gastroenterology and Hepatology, [2] University Hospitals Leuven, Belgium, Pneumology, [3] University Hospitals Leuven, Belgium, Pediatrics, [4] Medtronic, Jerusalem, Israel, R&D, [5] Coreva Scientific, Freiburg, Germany, Health Economics.

Introduction : Respiratory compromise (RC) is a state in which there is a high likelihood of decompensation into respiratory insufficiency, respiratory failure, respiratory arrest or death, but in which specific interventions (continuous monitoring and therapies) might prevent or mitigate decompensation. RC is the main cause of adverse events (AEs) occurring during procedural sedation. However, many clinicians are not aware of the incidence, the potential clinical consequences, and the value of monitoring in preventing AEs.

Aim : The study evaluated the incidence of respiratory-related AEs and interventions occurring during procedural sedation using World SIVA task force consensus definitions and the impact of capnography monitoring on these.

Methods : Our study was designed as a before-after quality improvement evaluation that received an ethics committee waiver. We compared data for patients admitted for scheduled procedures performed in the department with standard of care monitoring (control) to the data gathered for patients sequentially admitted for scheduled procedures that were monitored after full training with capnography both during the procedure and in recovery (intervention). Events were recorded during both the procedure and the recovery period. Collected data were deidentified and aggregated and included the ASA risk score, type of procedure, procedure duration, clinician ID and any indicated SIVA defined AEs and interventions that occurred. Incidence rates and relative risks for events and interventions were determined. The primary quality improvement endpoint was the change in total incidence of mild oxygen desaturation, severe oxygen desaturation, bradycardia, and tachycardia with capnography monitoring.

Results : Data were gathered between February 2018-June 2018, with 1,092 control patients and 1,044 intervention patients. In the control group there were on average 11.45 AEs per 100 procedures. In the intervention group there were on average 5.08 AEs per 100 procedures. The absolute difference between arms was -6.37 (95% [CI], -8.7 to -4.1) AEs per 100 procedures representing a 55.69% reduction ($p=0.0001$). The RR for a patient experiencing the primary outcome with use of capnography was: 0.43 (95% CI, 0.31 to 0.58). Nine escalations of care were reported in the control group with none reported in the intervention group. The relative risks of experiencing both AEs and interventions during recovery were reduced significantly in the capnography arm with a RR of 0.17 and 0.15, respectively for risk of AEs and need for intervention.

Conclusions : Capnography significantly reduced the incidence of respiratory AEs in real life use at a university hospital GI procedure suite.

- G05 -

TEN YEARS OF UPPER GASTROINTESTINAL BLEEDING IN A LARGE VOLUME EMERGENCY DEPARTMENT. M. Lomré (1), P. Mols (2), P. Kirkove (3), P. Eisendrath (4) / [1] ULB, Brussels, Belgium, Internal Medicine, [2] CHU Saint-Pierre, Brussels, Belgium, Department of Emergency, [3] CHU Saint-Pierre, Brussels, Belgium, Department of Medicine, [4] CHU Saint-Pierre, Brussels, Belgium, Department of Gastroenterology.

Introduction : Despite the frequent nature of upper gastrointestinal bleeding (UGIB) in medical emergency departments and the multiple scoring systems developed to predict the outcomes of these patients, the use of those risk scores is not generalised. As it was not in use systematically in our hospital, we wanted to evaluate their discriminating capacity for predicting different outcomes on our population with a retrospective study.

Aim : To analyse the etiologies of UGIB in a public hospital from the city centre of Brussels. To test two risk scores - Rockall Score (RS) and Glasgow-Blatchford Score (GBS) - in UGIB and to analyse how they perform for predicting outcomes.

Methods : Based on in-hospital records, we retrospectively studied 243 adults who were hospitalised from the emergency room for UGIB between 01/01/2004 and 31/12/2014 at the CHU St Pierre in Brussels, Belgium. We collected data regarding etiologies of UGIB, need of intervention (blood transfusion, endoscopic therapy, surgical treatment), the rebleeding rate and in-hospital mortality. We applied RS and GBS to respectively 238 and 242 patients.

Results : The most common etiology of UGIB was peptic ulcer (67,9%). No etiology was found for 12,4% of patients. Regarding interventions, 57,2% of patients required blood transfusion, 42,8% needed endotherapy and 7,4% underwent surgery. Rebleeding rate was 11,9%. Mortality was 6,6%. The RS had a greater discriminating capacity for mortality risk (AUC 0.82) than for predicting rebleeding rate (AUC 0.65). The GBS had a similar discriminating capacity for mortality (AUC 0.76) and for blood transfusion (AUC 0.86) and was less discriminant for the need of intervention (AUC 0.65). Applying the usual threshold for management of UGIB as outpatients (≤ 1), GBS identified correctly 106/107 patients who needed intervention, but one patient with a score of 0 needed transfusion and endoscopic therapy.

Conclusions : Despite major advances in management of UGIB, mortality remains significant in our inpatient population where peptic ulcer remains the principal cause of UGIB. The GBS is an interesting discrimination tool regarding mortality and for predicting the need of blood transfusion. The need of excluding patients with recent abdominal surgery from GBS for outpatient management assessment should be evaluated in larger prospective studies.

MANAGEMENT OF COMPLEX BILIARY LEAK BY ENDOSCOPIC DRAINAGE WITH TRANSMURAL OR TRANSPAPILLARY-TRANSFISTULARY ACCESS. L. Bromberg (1), A. Lemmers (2), M. Fernandez (2), V. Lucidi (3), D. Blero (2), O. Lemoine (2), J. Devière (2) / [1] Erasme Hospital, Brussels, Belgium, gastroenterology, [2] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology, Hepatopancreatology and Digestive Oncology, [3] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Abdominal Surgery.

Introduction : Biliary leak (BL) occurs most often after biliary tract surgery, laparoscopic cholecystectomy representing the leading cause. Drainage of biloma by surgical or radiologic drain is the priority to avoid sepsis. ERCP with biliary sphincterotomy and/or placement of a biliary stent or nasobiliary catheter represents the first therapeutic option with high clinical success. However, in some complex cases (high outflow of the leakage, hilar or intrahepatic leak or excluded ruptured hepatic segments) might resist to conventional treatment. Data on the place of endoscopic management of those complex cases to avoid complex redo-surgery has scarce.

Aim : We report our experience of biloma drainage with transpapillary/transfistulary (TP/TF) or EUS assisted-transmural (TM) access.

Methods : This is a retrospective analysis of prospectively collected data from January 2007 to December 2016 in the endoscopy unit of a tertiary care hospital. Biliary leakage diagnosis was based on imaging (biloma) or bile outflow from surgical drain. Patients having responded to conventional ERCP treatment were excluded from the analysis. Baseline characteristics, laboratory tests results, radiologic findings, procedural and follow up data were collected by reviewing patient's records, our endoscopic and radiologic database. TP/TF drainage was performed by the placement of double pigtail stent to drain the biloma through the leak during ERCP. For TM drainage, plastic DPT stents were placed under EUS control.

Results : We identified 30 patients (males 57%, median age 55 years) with BL (among 111 with BL having been treated in our unit during the same period) who were treated by TF/TP or TM drainage. BL resulted from cholecystectomy (26,7%), left or right hepatectomy (30%, 20%), liver transplantation (10%), partial liver segmentectomy (6,7%), or other (6,7 %). Pain and sepsis were the most common symptoms at presentation in 66% and 70% respectively. The drain, present in 90% of patients (from initial surgery (n=8), radiological percutaneous (n=16), from redo surgery (n=5)) had a mean daily bile flow before endoscopy of 300 cc (range 40 – 1600). The median duration between the date of surgery and endoscopic treatment was 54 (range 10 – 1144) days. TM drainage was performed in 14 patients by transgastric (8) or transduodenal (6) route with 86% requiring a unique session to achieve adequate EUS-drainage with one stent in 10 and 2 stents in 4. TP/TF drainage was performed in 16 patients, needing one, two or more interventions for adequate drainage in 75, 25 and 31% of the patients respectively, using one stent in 7 and 2 stents in 6 patients. Follow up was available for 21 patients alive or having not any order intervention at three months. Overall, in those patients, collection regression occurred in 52% of cases (TM: n=6; TF: n=5) and 57% (TM: n=6; TF: n=6) were free of sepsis and weaned from percutaneous drain. In a mean follow-up of 57 (1 – 333) months, biliary reconstructive surgery was necessary for 2 patients (TF: n=2) and percutaneous radiologic drainage for 1 patient. Six patients developed secondary biliary stricture that were calibrated by endoscopic or combined endoscopic/percutaneous stenting. Two patients died due to early complications related to endoscopic treatment (TF/TP: n=1, TM: n=1 (vascular/pericardial erosion by the stent), 3 patients died due to septic shock of biliary origin and 5 patients died following the progression of their neoplastic disease.

Conclusions : In patients with complex BL, transfistular/transpapillary or transmural drainage are technically feasible and might avoid redo-biliary surgery in more than 50% of the cases, helping in the resolution of biloma and the weaning of biliary drain. Knowing the risk of those procedures, this kind of treatment must be reserved and discuss in experienced tertiary centers.

AUTOMATED REAL TIME ENDOSCOPIC SCORING BASED ON MACHINE LEARNING IN ULCERATIVE COLITIS: RED DENSITY RELIABILITY AND RESPONSIVENESS STUDY. P. Bossuyt (1), S. Vermeire (2), M. Ferrante (2), T. Makino (3), G. De Hertogh (4), R. Bisschops (2) / [1] Imelda Hospital, Bonheiden, Belgium, Department of gastroenterology, [2] University Hospital, Gasthuisberg, Leuven, Belgium, Department of gastroenterology, [3] Pentax, Tokyo, Japan, Product development departement, [4] University Hospital, Gasthuisberg, Leuven, Belgium, Belgium, Department of Pathology.

Introduction : Endoscopic scoring in ulcerative colitis (UC) is subjective and has poor correlation with histological scoring. Histological remission predicts favourable long term outcome in UC. Operator independent automated digital scoring of endoscopic and histological inflammation in UC could provide an objective and predictive evaluation of remission.

Aim : The aim of this study was to test the operating properties of the Red Density score (responsiveness and reliability).

Methods : The Red Density (RD) system uses machine learning (ML) to calculate a score based on real time automatic extraction of pixel data from endoscopic images. This ML algorithm incorporates colour data and vascular pattern recognition. In this prospective study, consecutive patients with UC presenting at the IBD outpatient clinic with symptoms suggestive of a flare were included. At baseline and 8-14 weeks after treatment escalation we recorded endoscopic (Red Density score, Ulcerative colitis endoscopic index of severity [UCEIS], Mayo endoscopic subscore [MES]), clinical (total Mayo, PRO-2), histological data (Robarts histological index [RHI], Geboes score) and C-reactive protein. Investigators were blinded for the RD score. Correlation was tested between RD and clinical, biochemical, endoscopic, and histological scores (Spearman's rank correlation). Responsiveness was significant if standard effect size >0.8.

Results : Ten patients had 2 consecutive visits (M/F 4/6, median age 39y IQR 36-48). At baseline all patients had active endoscopic disease (median (IQR) UCEIS 4.5 (2.5-5); MES 2 (1.3-2)). Nine patients had a change in their endoscopic score after treatment compared to baseline. The median delta in UCEIS and MES was 3 (IQR 2-4) ($p=0.009$) and 1 (IQR 1-2) ($p=0.008$) respectively. A significant number of patients achieved clinical, endoscopic and histological remission after treatment (all $p<0.03$). Median RD score decreased significantly from baseline (166 to 58; $p=0.01$). RD correlated moderate with clinical outcomes ($r>0.65$, $p=0.001$), and strong with both endoscopic ($r>0.75$, $p<0.0001$), and histological scores ($r>0.75$, $p<0.0001$). The standardized effect size for RD was 1.22.

Conclusions : The automated digital endoscopic Red Density score correlates strongly with endoscopic, histological scores in UC. Red Density demonstrates an excellent sensitivity to change after treatment escalation. Red Density is an ideal operator-independent digital tool for the evaluation of endoscopic and histological disease activity in UC.

- G08 -

BLI AND LCI IMPROVE POLYP DETECTION RATE AND DELINEATION ACCURACY FOR DEEP LEARNING NETWORKS. T. Eelbode (1), C. Hassan (2), I. Demedts (3), P. Roelandt (3), E. Coron (4), P. Bhandari (5), H. Neumann (6), O. Pech (7), A. Repici (8), F. Maes (1), R. Bisschops (1) / [1] KU Leuven, Belgium, Medical Imaging Research Center, PSI, [2] Nuovo Regina Margherita Hospital, Rome, Italy, Gastroenterology, [3] KU Leuven, Belgium, Department of Gastroenterology and Hepatology, [4] Centre Hospitalier Universitaire Hotel Dieu, Nantes, France, Hepatogastroenterology, [5] Portsmouth Hospital, Portsmouth, United Kingdom (the), Solent Centre for Digestive Diseases, [6] University Medical Center Mainz, Mainz, Germany, First Medical Department, [7] Krankenhaus Barmherzige Brüder Regensburg, Regensburg, Germany, Department of Gastroenterology and Interventional Endoscopy, [8] Humanitas University, Milan, Italy, Digestive Endoscopy Unit.

Introduction : Current state-of-the-art automated polyp detection and delineation techniques use white-light imaging as their base modality. Studies have however suggested that polyp detection rates can be improved by using other modalities such as linked color imaging (LCI) from Fujifilm. This might be true for human observers, but it has not yet been investigated how an artificial intelligence (AI) system is influenced by the choice of modality.

Aim : The aim of this research is to investigate the influence of the chosen modality (WLI, BLI or LCI) on the performance of an AI system for polyp detection and delineation.

Methods : Complete pull-through colonoscopy videos from 120 patients are included with a total of 280 polyps for training, validation and testing of the system ($n = 176, 27, 77$ respectively with no overlapping patients). Shorter video clips containing the first apparition of each polyp are extracted and for each clip, only a few frames are annotated by three individual experts. These 758 single-frame manual annotations are automatically propagated over the entire clip using dense object tracking. The resulting, much larger annotated dataset of 40887 images is then used to train a recurrent convolutional neural network (CNN) for polyp detection and delineation. Frame-level sensitivity and specificity are reported for evaluation of the detection power of the network. For delineation accuracy, the Dice score is used which is a measure for the amount of overlap between a delineation map and its ground truth. The analysis is done for WLI, BLI (blue light imaging) and LCI.

Results : The sensitivity is highest for BLI with also a significant increase for LCI (sens=0.81, 0.92, 0.85 for WLI, BLI and LCI respectively). Specificity shows the same trend (spec=0.76, 0.85, 0.82 respectively). This clearly indicates a higher performance for polyp detection with LCI and especially BLI when compared to using WLI. Similarly, for delineation, BLI has the highest accuracy (Dice score=0.69, 0.76, 0.63 respectively for WLI, BLI and LCI). For this task, LCI is inferior to WLI. Pairwise t-tests show that all differences are significant with a p value <0,00001 (significance level of 0,05).

Conclusions : The choice of modality has a significant impact on the detection and delineation performance of an AI system. We show that our network performs best for both tasks on BLI and that LCI has a superior detection, but inferior delineation power compared to WLI.

- G09 -

GASTRIC PER ORAL ENDOSCOPIC PYLOROMYOTOMY (G-POEM): A RETROSPECTIVE SINGLE-CENTER EXPERIENCE. Y. Mourabit (1), D. Blero (1), V. Huberty (1), M. Arvanitakis (1), J. Devière (1), H. Louis (1) / [1] Erasme Hospital, Brussels, Belgium, Gastroenterology.

Introduction : Gastroparesis is a rare, chronic heterogeneous disorder associated with high morbidity, reduced quality of life. Patients suffer from a variety of symptoms including nausea, vomiting, bloating, early satiety, abdominal pain and/or weight loss, symptoms being often refractory to medical management. The major etiologies include diabetes, idiopathic and post-surgical. Physiopathology of gastroparesis is complex and involves delayed gastric emptying increased pyloric tone. Among therapies aim to diminish pyloric tone, endoscopic gastric per oral myotomy has been recently proposed for patients with refractory symptoms.

Aim : To evaluate the safety and the efficacy of G-POEM as a treatment of patients with gastroparesis and refractory symptoms.

Methods : All patients who were intended to benefit from G-POEM in our center from January 2015 to November 2018. Symptoms were assessed with the Gastroparesis Cardinal Symptoms Index (GCSI) score. Gastric Emptying was evaluated with scintigraphy (GES) (half gastric emptying time (HGET), Retention Percentage at 2 Hours (RPH2) when available. Statistical evaluation was carried out using the software SPSS. A statistical difference is determined with the Wilcoxon Signed Ranks Test, with $P < .05$ considered as significant. Data are presented as medians with minimum and maximum.

Results : 23 patients were treated under general anaesthesia with endotracheal intubation with a median length of myotomy of 2cm (1-3, n=12). GES was delayed in all patients, median HGET was 143.5min (101-802, n=13) and RPH2 58.5% (40-104, n=14). Median follow-up was 3 months (1-24, n=22). Aetiologies were diabetic in 13% of patients (n=3), post-surgical in 30% of patients (n=7), idiopathic in 30% of patients (n=7), post oesophago-gastrectomy in 26% (n=6). Median duration of symptoms was 26 months (2-149). Median age was 55 years (17-73, n=23), with 74% of female (n=17) and 26% of male subjects (n=6). Previous therapies included Botox injection in 39% of patients (n=9), and Surgical jejunostomy in 13% of patients (n=3). G-POEM was completed successfully in 22 patients (95.65%) with one failure due to transmural section at mucosal incision with no access to submucosal space. They were 3 immediate complications and no delayed complications (1 bulbar perforation, 1 gastric perforation and 1 hemorrhage) all managed endoscopically. Median GCSI before and after treatment were 4 (2.78-5, n=11) and 2.11 (0.44-4.44, n=13). GCSI was compared before and after treatment in 10 patients and were significantly improved ($p=0.022$). GES were obtained in 14 patients at 3 months (1-10), with a significant reduction of RPH2 and HGET ($p=0.003$ and 0.016).

Conclusions : G-POEM is a technically feasible and safe procedure. These retrospective data suggest that G-POEM is a promising new treatment for patients with refractory gastroparesis, for who the therapeutic options are very limited.

- G10 -

OUTCOMES OF ENDOSCOPIC FULL THICKNESS RESECTION (EFTR) USING THE FULL THICKNESS RESECTION DEVICE (FTRD): FIRST BELGIAN EXPERIENCE. C. Snauwaert (1), P. Deprez (2), H. Piessevaux (2) / [1] AZ Sint-Jan Brugge-Oostende, Brugge, Belgium, Hepatology and Gastroenterology, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Hepatology and Gastroenterology

Introduction : Endoscopic Full Thickness Resection (EFTR) using the full thickness resection device (FTRD) enables en-bloc resection of lesions involving or originating from the deeper layers of the intestinal wall which would otherwise require surgical removal. We present the first Belgian EFTR-series using the FTRD and delineate feasibility and early outcomes of this procedure.

Aim : To assess efficacy, safety and early outcomes of EFTR using the FTRD and identify possible risk factors for technical difficulty.

Methods : Retrospective analysis of a prospectively collected database of patients scheduled for EFTR using the FTRD system between January 2015 - November 2018. Main endpoints were technical success, specimen size, R0 resection, and adverse events.

Results : 23 consecutive patients were identified across two centers (10/13). Median age of patients was 71 years (IQR 34-78). Lesions were located throughout the gastrointestinal tract: ileal pouch (1), appendix base adenoma (1), caecum (2), ascending colon (2), hepatic flexure (3), transverse colon (1), splenic flexure (3), descending colon (3), sigmoid colon (3), rectum (3) and gastric antrum (1). Indications for EFTR included gastric submucosal neuro-endocrine tumor (NET) (1), residual rectal NET after endoscopic resection (1), appendix base adenoma (1), central adherence (fibrosis) during endoscopic submucosal dissection (ESD) at the splenic flexure (1), earlier attempt at endoscopic mucosal resection (EMR) with non-lifting sign (4), residual adenomatous tissue after EMR (4), incomplete endoscopic resection of a malignant polyp (3) and endoscopic findings suggestive of deep submucosal invasion (8). In all patients the target lesion could be reached with the FTRD. Successful EFTR was achieved in 96% of patients (22/23). Median specimen size was 22.4 mm (range 11-35). R0 resection was achieved in 87% of patients (20/22). Post-procedure complications occurred in 2 patients of which 1 delayed bleeding (successfully endoscopically treated) and 1 patient required surgery for intra-procedural perforation salvage (FTRD maldeployment). Two FTRD procedures were performed under conscious sedation (midazolam/alfentanil) without any complications. The majority of lesions (14/22) contained advanced histologic features: high-grade dysplasia / intramucosal carcinoma (4), pT1 (9) and one pT2 lesion. In 3 of these patients, additional surgery was performed (unfavorable histopathology; risk of lymph node metastasis) and no residual tumor or lymph node metastasis could be detected.

Conclusions : EFTR using the FTRD appears to be feasible and efficacious in the resection of lesions of up to 30 - 35 mm in diameter and may offer a minimally invasive approach for radical resection of these lesions as an alternative to surgery in selected patients. Safety is a concern and more long-term follow-up data are awaited.

- G11 -

LONG TERM RATES OF SURGERY AND ADENOMA RECURRENCE ARE SIMILAR FOR LATERALLY SPREADING LESIONS RESECTED EN BLOC OR BY PIECEMEAL ENDOSCOPIC MUCOSAL RESECTION. D. Tate (1), H. Awadie (2), L. Desomer (3), M. Sidhu (2), N. Burgess (2), L. Hourigan (4), A. Moss (5), S. Raftopoulos (6), R. Singh (7), G. Brown (8), M. Bourke (2) / [1] UZ Gent, Gent, Belgium, Gastroenterology and Hepatology, [2] Westmead Hospital, Australia, Gastroenterology and Hepatology, [3] AZ Delta, Roeselare, Belgium, Gastroenterology and Hepatology, [4] Gallipoli Medical Research Institute, Australia, Gastroenterology and Hepatology, [5] Western Hospital, Australia, Gastroenterology and Hepatology, [6] Sir Charles Gairdner, Australia, Gastroenterology and Hepatology, [7] Lyell McEwan Hospital, Australia, Gastroenterology and Hepatology, [8] The Alfred Hospital, Australia, Gastroenterology and Hepatology.

Introduction : Endoscopic mucosal resection (EMR) allows safe and effective resection of large laterally spreading lesions ≥ 20 mm (LSL). Adenoma recurrence is commonplace when resection is performed piecemeal (pEMR). En bloc EMR (eEMR), however, has been shown to achieve low adenoma recurrence rates but long term outcomes are unknown.

Aim : Establish the long term outcomes of LSL resected en bloc versus those resected piecemeal.

Methods : Over 9 years to April 2017 analysis of LSL resected by EMR from a prospectively collected database at 8 Australian Tertiary Referral Centres was performed. LSL ≤ 25 mm in the left colon and ≤ 20 mm in the right colon were included. Multiple LSL in the same patient were excluded. Standard inject and resect EMR was performed. LSL resections were identified as piecemeal or en bloc (single snare resection) and their outcomes were compared. Scheduled surveillance colonoscopy was performed at desired intervals of 4-6 months (surveillance colonoscopy 1 - SC1) and 18 months after EMR (SC2).

Results : 587 LSL were included of which 267 (45.5%) were resected en bloc, with histologic clear margins in 80.4%. Lesion characteristics were broadly similar between the groups. Neither colonic location nor morphology predicted en bloc resection. En bloc resections took less time, median 10 versus 20 minutes, $p < .001$. Muscularis propria injury ($P=.038$) and delayed bleeding ($P=.067$) were more common with en bloc resection. Recurrence at SC1 (median 5.0 months) was detected at 5/195 (2.6%) eEMR scars and 23/320 (9.3%) pEMR scars, $P = .004$. Surgery at SC1 for recurrence unable to be removed endoscopically was required in 3/195 (1.5%) for eEMR lesions versus 2/320 (0.6%) for pEMR, $P=.659$. Recurrence at SC2 (median 18.0 months) was detected at 1/126 (0.8%) eEMR scars versus 7/130 (5.4%) pEMR, $P = .025$. Surgery at SC2 for defiant recurrence was required in 0/126 (0%) eEMR lesions versus 1/130 (0.8%) pEMR, $p=1.000$.

Conclusions : En bloc EMR is quicker to perform, but is higher risk for delayed bleeding and perforation versus pEMR for colonic LSL ≤ 25 mm. Recurrence rates are higher for LSL resected using pEMR than eEMR but the requirement for surgery is the same predominantly due to the ability to treat recurrence endoscopically. Therefore, particularly in an era of adjuvant techniques which substantially reduce recurrence, en-bloc resection need not be pursued at all costs for predicted-benign disease.

- G12 -

COLD SNARE POLYPECTOMY IS SAFE YET UNDER-UTILISED: AN ANALYSIS OF 281,194 POLYPECTOMIES BY UK ENDOSCOPY TRAINEES OVER 9 YEARS. D. Tate (1), D. Wheatley (2), J. Anderson (2), R. Valori (2), P. Dunkley (2) / [1] UZ Gent, Gent, Belgium, Gastroenterology, [2] Gloucestershire Hospitals NHS Foundation Trust, United Kingdom (the), Gastroenterology and Hepatology.

Introduction : Multiple techniques exist for the management of colorectal polyps. Recent (2017) ESGE guidelines defined an evidence based approach to the optimal polypectomy technique for different sizes of polyps.

Aim : We examined polypectomy practice amongst United Kingdom endoscopy trainees with reference to these guidelines.

Methods : The ESGE polypectomy guideline 2017 suggests polyps <10 mm should be removed using cold snare polypectomy (CSP) or cold biopsy forceps (CBF) [≤ 3 mm only], 10-19mm using endoscopic mucosal resection (EMR) or hot snare polypectomy (HSP) and 20mm or larger using EMR. The JETS database is a prospective record of trainee colonoscopic procedures in the United Kingdom and its use during training is mandatory for accreditation. Data is entered by trainees on consecutive endoscopic procedures. Adverse events were classified as delayed bleeding or delayed perforation. We retrospectively analysed procedures entered into the JETS database from January 2008 to December 2017 for polypectomy technique and compared this to the guideline.

Results : 291,778 polypectomies were performed in 176,569 procedures by 3395 trainees over the study period. 10,584 polypectomies were missing data. 281,194 polypectomies were analysed. Of 250,783 polyps < 10mm in size removed, 29.5% were performed using CBF, 27.9% by CSP, 25.1% by HSP, 9.5% by hot biopsy forceps (HBF), and 8.0% by EMR. Of 26,605 polyps 10-19mm in size, 55.3% were removed by HSP, 31.0% by EMR and 3.5% by CSP. 8.4% of lesions were biopsied and not removed. Of 3806 polyps \geq 20mm in size, 39.4% were removed by EMR, 36.3% by HSP, 1.1% were removed by CSP and 21.9% of these lesions were biopsied and not removed. Overall, adherence to the guideline was observed in 154,948 polypectomies (55.1%). Nurse endoscopists were more adherent (61.7%), versus physicians (57.9%) versus surgeons (44.3%), $p < .001$. Of 219 (0.1%) adverse events reported amongst all polypectomies, 50.8% were amongst HSP, 19.2% EMR, 16.9% CSP and 12.7% after HBF, $p < .001$. Of 20 delayed perforations (event rate 0.01%), 55% were due to EMR, 30% to HSP and 15% to HBF. No perforations resulted from CSP. 0.03% of all polypectomies resulted in unplanned hospital admission. Of these admissions 45.1% were after EMR, 35.1% after HSP and 6.4% after CSP, $p < .001$.

Conclusions : Cold snare polypectomy is under-utilised for diminutive polypectomy, despite its proven safety and efficacy; its use amongst trainees should be promoted in line with ESGE guidance. Trainees are likely to follow the example of their trainers and, as such, this study likely provides an insight into current polypectomy practice in the wider UK endoscopic community. Trainees in the United Kingdom predominantly remove diminutive polyps with extremely low reported rates of adverse events, but do not often perform more complex polypectomy.

- G13 -

EOSINOPHILIC ESOPHAGITIS: CLINICAL, ENDOSCOPIC AND HISTOLOGIC LONG-TERM FOLLOW-UP: A SINGLE-CENTRE RETROSPECTIVE COHORT AND CROSS-SECTIONAL STUDY. L. Crapé (1), G. Cornelis (2), F. de Clerck (3), D. De Looze (2) / [1] UZ Gent, Gent, Belgium, Gastro-enterology, [2] UZ Gent, Gent, Belgium, Gastro-enterology, [3] AZ Sint-Lucas, Ghent, Belgium, Gastro-enterology.

Introduction : In the past 15 years eosinophilic esophagitis (EoE) has evolved from being a rare disease to being considered the most important cause of dysphagia and food impaction in children and adolescents. Up until now, little is known about its natural history. Retrospective data suggest progression from an inflammatory to a fibrostenotic disease type in a large proportion of the patients. Standard treatment consists of a topical corticosteroid (TC), a proton pump inhibitor (PPI) or an elimination diet (ED) but rapid relapse is seen after stopping the treatment. There are however no data about long-term treatment and its effect on preventing complications.

Aim : The aim of this study is to evaluate long-term clinical, endoscopic and histological data in patients with EoE, and to assess their current treatment and follow-up in daily clinical practice.

Methods : First, a single-centre retrospective cohort study was conducted including data from patients diagnosed with EoE at the University Hospital of Ghent between 2004 and 2017. Data regarding demographics, symptoms, endoscopic image, histology and management were collected from the medical records. Second, we conducted a cross-sectional study design using questionnaires by mail to collect information regarding current symptoms, treatment and follow-up. All patients receiving a questionnaire were adults (>18 years). Missing data were collected by telephone interviews. Statistical analyses were performed using SPSS Statistics 25. The study was approved by the ethics committee.

Results : We included 56 patients diagnosed with EoE. The mean age at diagnosis was 34.3 years (SD \pm 14.1), with a mean diagnostic delay of 6.1 years (SD \pm 8.3). Dysphagia (83.9%) and impaction (61.8%) were the most frequent symptoms. At the time of diagnosis, endoscopic abnormalities were seen in 73.2% of the patients with tracheal folds and linear furrows being the most frequent. Esophageal stenosis was seen in 16.1%, these patients had a mean diagnostic delay of 4.5 years (SD \pm 5.0). We found no difference in prevalence of strictures between patients with a diagnostic delay < 5 years compared to a diagnostic delay of > 10 years. Initial treatment included PPI (47.3%), ED (18.2%), TCS (12.7 %) or a combination of PPI and TCS (3.6%). Three patients (5.3%) needed a dilation. A second treatment was started in 41.1% of the patients of which 44% were prescribed a TCS, 39% an ED, 4% a PPI and 4% a combination of PPI and TCS. Cumulatively, we saw a favourable clinical effect in 50% of patients on PPI, in 54.5 % of patients on TCS and in 85% of patients on ED. Histologic remission was seen in 21% of patients on PPI, in 54% of patients on TCS and in 60% of patients on ED. A follow-up endoscopy was performed in 48.2% of the patients, with a mean of 3.72 years (SD 4.1) after diagnosis. In the majority of patients (78.6%) similar abnormalities as in the initial endoscopy were described. We saw endoscopic normalization in 14.3% and stricture formation in 2 patients (7.1%). Both of these patients had a follow-up time longer than 10 years. Over the entire course, endoscopic dilation was performed in 5 patients (8.9%). The response rate at the questionnaire was 83.9%. At that time, 34% of patients were on maintenance therapy with PPI, only 2 patients (4.2%) were on maintenance therapy with a TCS. Long term ED were sustained in 42.2% of all patients. 46.8% reported dysphagia 1-3 times/ week, 6.4% reported 4-6 times/ week, 2.1% reported daily dysphagia. Behavioural adaptations were reported in 63% for meat, 44.7% for bread and 8.7% for fluids. However, we found no statistical differences between reported symptoms or behavioural adaptations between patients with or without maintenance therapy. Long-term follow-up was planned in 35% of the patients.

Conclusions : EoE seems a benign condition but it does cause chronic symptoms in the majority of patients. PPIs seem to be the most sustainable medical treatment, given the safety concerns of long-term corticoids. However, the best

clinical and histologic effects in our study were seen with elimination diets, as sustained by almost half of the patients. We could not detect statistically significant differences between reported symptoms or behavioural adaptations between patients with or without maintenance therapy. During 14 years of follow-up time, only 2 patients developed strictures. Only in 35% of the patients long-term follow-up was planned.

- G14 -

A DEDICATED COMPETENCY-BASED TRAINING PROGRAM IN ENDOCOPIC RESECTION ALLOWS SAFE AND EFFECTIVE RESECTION OF COMPLEX LATERALLY SPREADING LESIONS AFTER 12 MONTHS. M. Sidhu (1), I. Bar-Yishay (1), M. Bourke (1), D. Tate (2) / [1] Westmead Hospital, Australia, Gastroenterology and Hepatology, [2] UZ Gent, Gent, Belgium, Gastroenterology and Hepatology.

Introduction : No formal training pathways for endoscopic mucosal resection (EMR) currently exist and training is often ad-hoc and sporadic. Many endoscopists practice EMR without formal training. This may contribute to incomplete polyp resection and referral of large benign colorectal neoplasia to surgery.

Aim : We aimed to investigate the impact of a dedicated 12-month EMR training program on trainee competency.

Methods : Prospective data relating to technical aspects of EMR and outcomes was collected from consecutive directly-supervised procedures commenced by five trainees over a 12-month period at a tertiary endoscopic resection centre. All trainees had achieved appropriate competency in colonoscopy (at least 200 independent procedures prior to their training year of which at least 50 procedures involved basic polypectomy) and undertook a four-week observation period prior to starting cases. Data was analysed in two cohorts divided by procedures performed in the first or second six months of the program.

Results : Five trainees (median age – 31yrs) performed 98 EMRs in 98 patients over 12 months. Median lesion size in the first half was 30mm (interquartile range [IQR] 25-40) and 35mm (IQR 25-50) in the second. The complexity of LSL increased in the second half of the cohort [SMSA 4 end versus start, 47.2% (26/55) versus 32.5% (14/43)]. Other important lesion characteristics did not vary between the halves of the cohort. The ability to competently perform dynamic submucosal injection and complete specimen retrieval after EMR was significantly more likely in the second six months of training as compared to the first (86.8% vs 54.8%, $p=0.001$ and 88.9% vs 60.5%, $p=0.002$ respectively). Trainees were significantly more likely to independently complete greater than 50% of the EMR procedure in the second six months of their training as compared to the first (81.8% vs 51.2%, $p=0.001$, odds ratio [OR] – 4.3 [1.7-10.7], $p=0.002$). Need for consultant intervention was also significantly less likely in the second half of the training period (62.8% vs 40%, $p=0.004$). Despite the involvement of a trainee and the complexity of the lesions attempted, technical success (96.9%) and delayed bleeding (10.0%) were similar to resections performed by experts from the outset.

Conclusions : Colonoscopists competent in diminutive polypectomy can be trained to perform EMR of complex colorectal lesions safely and without detriment to overall outcomes. Key aspects of this programme include a focussed, intensive period of training (>6 months) with competency-based teaching and introduction of sequentially more complex lesions using a validated scoring method. This study may provide a framework for the development of a structured, competency based framework for endoscopists to train in advanced tissue resection.

- G15 -

NATURAL HISTORY OF BILIARY CAST SYNDROME AFTER LIVER TRANSPLANTATION: A PROSPECTIVE CHOLANGIOGRAPHIC EVOLUTION STUDY. A. Hadeji (1), M. Pezzullo (2), S. Dept (1), O. Le Moine (1), J. Devière (1), T. Gustot (1), C. Moreno (1), N. Boon (1), D. Degré (1), V. Lucidi (3), A. Lemmers (1) / [1] C.U.B. Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium, Department of Gastroenterology, Hepatopancreatology and Digestive Oncology, [2] C.U.B. Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium, Radiology Department, [3] C.U.B. Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium, Abdominal Surgery Department.

Introduction : Biliary cast syndrome (BCS) is a rare complication after liver transplantation (LT) defined as material molded into the bile ducts and associated with ischemic cholangitis. Knowledge on cholangiographic features and endoscopic management of BCS is scarce.

Aim : We sought to review the radiologic and cholangiographic features of BCS.

Methods : Records of the prospectively collected database of patients having been treated by liver transplantation in Erasme hospital from 12/2004 to 12/2014 were analyzed to identify patients having biliary complications (BC). After the exclusion of those having altered anatomy or no stricture, their cholangiograms and magnetic resonance cholangiography (MRCP) were systematically reviewed identifying patients with BCS. It was defined as intrabiliary material associated to filling defect during cholangiography in the supra-anastomotic portion of the biliary tree with features of biliary injury. Three types of BC were identified: BCS, anastomotic (AS) and non-anastomotic strictures (NAS). Clinical, endoscopic and radiological data of those patients were reviewed.

Results : BC were present in 86 (27%) of the 313 patients (70% male; mean age, 61±7 years). Fourteen cases (4.6%) identified to have a BCS were treated by ERCP. There was no statistical difference in patient demographics, delay between LT and BC in the three groups. Pre-therapeutic MRCP was available in 12/14 cases with none having been described as BCS. The revision of these MRCP disclosed the following features: T1 hypersignal material filling the duct was present in 11, a “duct-in-a-duct” picture in 8 and an aneurysm-like saccular dilation of the bile duct in 3 of the 12 cases, respectively. On initial ERCP, 8 of the 14 patients had no stricture. A saccular aneurysmal or moderate biliary dilatation containing cast was present in 6 and 5 patients respectively. It was possible to obtain a complete cast extraction by ERCP in 12 of the 14 cases in a median of 2 (1-7) ERCP sessions in a median period of 3 (1-22) months. Only one of the 12 patients with cast completely extracted presented with cast recurrence in the follow-up (8%). Eleven of the 13 patients (85%) for who ERCP follow-up was available presented an evolution with secondary biliary strictures treated with multiple plastic stents. Stricture calibration was obtained in 10 of them (90%) after a median of 5 (4-9) ERCP sessions on a median of 12 (5-19) months treatment period. In 4 of the 10 patients, we observed stricture recurrence at 14 (1-84) months of stent retrieval. New stenting sessions for stricture recurrence calibration were performed by a median of 6 (4-10) ERCP in 22 (12-42) months for those patients with 3 of them (75%) obtaining stricture calibration and one partial hilar calibration and left excluded bile ducts without clinical counterpart. At the end of a median follow-up of 58 months, we observed a lower overall survival (42,9% (BCS) Vs 83,3%(AS) Vs 68,8% (NAS), p value of log rank tests = 0.035) and a lower re-transplant-free survival (42,9 % (BCS) vs 80,6% (AS) vs 56,3% (NAS), p value of log rank tests=0.025) for patients with BCS compared to those without.

Conclusions : Biliary cast syndrome is a rare complication of liver transplantation and is associated to specific radiological features. Complete cast extraction is possible by ERCP. The prognosis of those patients is poorer compared to the overall patients presenting biliary complications after LT.

- G16 -

IS THE SHORT-TYPE SINGLE-BALLOON ENTEROSCOPE USEFUL FOR ENTEROSCOPY-ASSISTED ERCP IN PATIENTS WITH SURGICALLY ALTERED ANATOMY? T. Moreels (1), E. Motté (1), P. Deprez (1), H. Piessevaux (1) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Hépatogastroentérologie.

Introduction : Roux-en-Y reconstructive surgery of the small bowel excludes the afferent limb and the biliopancreatic system from conventional endoscopic access. Therefore, postoperative problems in the biliopancreatic system are often dealt with surgically. Balloon-assisted enteroscopy allows therapeutic endoscopic retrograde cholangiopancreatography (ERCP) in these patients, avoiding rescue surgery. Nowadays, several types of balloon-assisted enteroscopes are available to perform ERCP in patients with surgically altered anatomy.

Aim : To investigate whether the short-type single-balloon enteroscope SIF-H290S can be used for ERCP in patients with surgically altered anatomy, and to define which type of surgery is particularly (un)suitable for the use of the short-type SIF-H290S, in comparison with the long-type SIF-Q180 and XSIF-180JY single-balloon enteroscopes (SBE).

Methods : The SIF-H290S has a working length of 152 cm in comparison to the 200 cm of the long-type SBE. Therefore, SIF-H290S allows the use of conventional ERCP accessories, which are not compatible with the long-type SBE. Between May and November 2018, 31 consecutive enteroscopy-assisted ERCP procedures were initiated with the SIF-H290S SBE. In case of failure to reach the bile duct, the short-type SBE was replaced by a long-type SBE. Technical success related to the type of SBE and the type of surgical reconstruction was recorded.

Results : 31 ERCP procedures were initiated with the SIF-H290S in 26 patients. Male/female ratio was 54/46% with a mean age of 60±5 years and 55±5 years respectively, ranging from 22 to 91 years. Total technical ERCP success was 84% (26/31 procedures) combining both short-type and long-type SBE. However, only 21 procedures (68%) were completed with the SIF-H290S, 5 failures were completed with a long-type SBE, and 5 were technically unsuccessful with both the short- and long-type SBE (16% failure). All failures were due to failure to reach Vater's papilla or the biliary anastomosis. Surgical reconstructions were Roux-en-Y hepaticojejunostomy (including liver transplantation) in 13 (42%) procedures, Whipple's resection with and without Roux-en-Y in 5 (16%), gastrojejunostomy in 5 (16%), Roux-en-Y total gastrectomy in 4 (13%) and Roux-en-Y gastric bypass in 4 (13%). Of the 13 ERCP procedures in Roux-en-Y hepaticojejunostomy patients SIF-H290S technical success was only 54% and an additional 2 (15%) were completed with a long-type SBE. Total failure rate in Roux-en-Y hepaticojejunostomy was 31%. Total technical success rate was 5/5 (100%) in patients with Whipple's resection with and without Roux-en-Y, of whom 80% was completed with the SIF-H290S. All 5 procedures in patients with a gastrojejunostomy were successfully completed with the SIF-H290S (100%), as were all 4 procedures in patients with Roux-en-Y total gastrectomy (100%). In patients with Roux-en-Y gastric bypass, only 1 (25%) was successfully completed using the SIF-H290S, and 2 (50%) with a long-type SBE. These results show that ERCP failure using the short-type SIF-H290S is related to the presence of either a normal stomach (Roux-en-Y hepaticojejunostomy) or long-limbs (Roux-en-Y gastric bypass). However, the short-type SIF-H290S allows the use of conventional ERCP accessories, whereas these are not compatible with the long-type SIF-Q180 and XSIF-180JY.

Conclusions : The short-type SIF-H290S SBE is particularly useful to perform ERCP in patients with surgically altered

anatomy since it is compatible with most conventional ERCP accessories. However, technical failure to reach the bile duct is related to the presence of a normal stomach (Roux-en-Y hepaticojejunostomy) or long Roux-en-Y limbs (Roux-en-Y gastric bypass). For these surgical reconstructions the SIF-H290S is often too short. In those cases a long-type SBE is mandatory, which implicates accessories adapted to the length and width of the SBE working channel.

- G17 -

PATIENT RADIATION EXPOSURE DURING ENTEROSCOPY-ASSISTED ERCP. T. Moreels (1), O. De Ronde (1), P. Deprez (1), H. Piessevaux (1) / [1] Cliniques universitaires Saint-Luc, Brussels, Belgium, Hépatogastroentérologie.

Introduction : Radiation exposure implicates risks to both the patient and the endoscopy personnel. ESGE guidelines provide data on patient radiation exposure during conventional ERCP. However, no data are currently available on patient radiation exposure during enteroscopy-assisted ERCP in patients with surgically altered anatomy.

Aim : To provide data on radiation exposure in patients with surgically altered anatomy undergoing enteroscopy-assisted ERCP (EA-ERCP) during a 3-months registration period in comparison with conventional ERCP (C-ERCP) data.

Methods : 20 EA-ERCP procedures were compared with 53 C-ERCP procedures. Data on patient and procedure characteristics were collected as well as radiation data: fluoroscopy time, total radiation dose and dose-area product (DAP).

Results : Mean age in the EA-ERCP group was 58 ± 5 years vs. 66 ± 2 years in the C-ERCP group ($p=0.105$) with a general M/F ratio of 67/33%. Surgical reconstructions were Roux-en-Y hepaticojejunostomy, total gastrectomy, gastric bypass and Whipple's resection. EA-ERCP indications were biliary, whereas C-ERCP indications were both biliary and pancreatic. Mean fluoroscopy time was comparable in both groups (358 ± 28 sec vs. 350 ± 40 sec, $p=0.815$), as was total mean radiation dose with a tendency to be lower in the EA-ERCP group (83 ± 9 mGy) as compared to the C-ERCP group (97 ± 10 mGy, $p=0.449$). However, DAP was significantly higher in the EA-ERCP group (2104 ± 187 $\mu\text{Gy} \cdot \text{m}^2$ vs. 1464 ± 117 $\mu\text{Gy} \cdot \text{m}^2$, $p=0.006$), as is the total procedure time (82 ± 7 min vs. 41 ± 3 min, $p<0.001$). These results indicate that C-ERCP procedures are more complex needing magnified fluoroscopy, whereas EA-ERCP procedures take more time for enteroscope insertion under wide field fluoroscopic guidance (as shown by increased DAP) with less complex ERCP manipulation (as shown by lower total dose).

Conclusions : Radiation exposure in EA-ERCP is different as compared to C-ERCP: EA-ERCP takes longer with a higher DAP, but with a lower total radiation dose. This is explained by the need of fluoroscopy during enteroscope insertion (higher DAP) to perform less complex ERCP procedures (lower total dose).

A VEDOLIZUMAB SPECIFIC FOUR-GENE COLONIC SIGNATURE ACCURATELY PREDICTING FUTURE ENDOSCOPIC REMISSION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE. B. Verstockt (1), S. Verstockt (2), P. Sudhakar (3), J. Dehairs (4), H. Blevi (3), G. Van Assche (3), S. Vermeire (3), M. Ferrante (3) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Department of Chronic Diseases, metabolism and ageing, [2] Laboratory for Complex Genetics, KU Leuven, Belgium, Department of Human genetics, [3] Translational Research Center for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Department of Chronic Disease, Metabolism and Ageing, [4] Laboratory of Lipid Metabolism and Cancer, KU Leuven, Belgium, Department of Oncology.

Introduction : Vedolizumab, a monoclonal antibody targeting alpha4beta7 integrin and mainly inhibiting gut lymphocyte trafficking, has been approved for the treatment of both Crohn's disease (CD) and ulcerative colitis (UC). Due to the increasing availability of therapeutic compounds in inflammatory bowel disease (IBD), predictive biomarkers are urgently awaited in order to help clinicians decide between anti-TNF, vedolizumab or other therapies.

Aim : We aimed to identify baseline transcriptomic profiles in inflamed colonic biopsies predicting vedolizumab-induced endoscopic remission.

Methods : We obtained inflamed colonic biopsies from 31 patients (20 UC, 11 CD) prior to initiation of vedolizumab. Similarly, inflamed colonic biopsies (15 UC, 9 CD) were collected from 24 patients initiating anti-TNF therapy (Table 1). RNA was extracted and single-end RNA sequencing was performed using Illumina HiSeq4000. Normalization and differential expression was done using DESeq2 R package. Pathways were analysed with Ingenuity Pathway Analysis (IPA). Using randomized generalized linear modelling (RGLM), a predictor for vedolizumab-induced endoscopic remission (absence of ulcerations at month 6 for CD; Mayo endoscopic sub-score ≤ 1 at week 14 for UC) was identified in a randomly generated test cohort (n=20) and validated in 11 independent samples. Through unsupervised consensus clustering, we validated the marker in a publicly available microarray dataset (GSE73661), and studied vedolizumab specificity in the anti-TNF treated cohort.

Results : Forty-four genes (25 down, 19 up) were significantly differently expressed between future vedolizumab remitters and non-remitters. Involved pathways included glucocorticoid receptor signalling, differential regulation of cytokines in intestinal epithelial cells, granulocyte adhesions and diapedesis. Using these 44 differentially expressed genes as input for the RGLM modelling, we identified a 4-gene signature which could accurately split remitters and non-remitters in both the discovery (accuracy 90.9%, p=0.02) and validation (100%, p=0.006) set. Using the same 4-gene signature we could accurately discriminate prospective future remitters from non-remitters in a publicly available microarray data set of 13 open-label vedolizumab treated UC patients (84.6%, p=0.02). In contrast, this 4-gene signature was not predictive for anti-TNF induced endoscopic remission (62.5%, p=0.65).

Conclusions : We identified and validated the first, vedolizumab-specific predictive 4-gene expression signature which may guide treatment strategy in IBD patients with colonic involvement.

AN INTEGRATED MULTI-OMICS BIOMARKER PREDICTING ENDOSCOPIC RESPONSE IN USTEKINUMAB TREATED PATIENTS WITH CROHN'S DISEASE. B. Verstockt (1), P. Sudhakar (2), B. Creyns (3), S. Verstockt (4), J. Cremer (3), W. Wollants (2), S. Organe (2), T. Korcsmaros (5), M. Madgwick (5), G. Van Assche (2), C. Breynaert (3), S. Vermeire (2), M. Ferrante (2) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Department of Chronic Diseases, metabolism and ageing, [2] Translational Research Center for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing, [3] Laboratory of Clinical Immunology, KU Leuven, Belgium, Department of Microbiology and Immunology, [4] Laboratory for Complex Genetics, KU Leuven, Belgium, Department of Human Genetics, [5] Earlham Institute, United Kingdom.

Introduction : Ustekinumab (UST), an anti-IL12/23p40 monoclonal antibody, has been approved for Crohn's disease (CD). Due to the increasing availability of therapeutic compounds in CD, predictive biomarkers are urgently needed in order to help clinicians to choose the best treatment with the highest likelihood of therapeutic success.

Aim : The aim of this study was to identify baseline predictors of response using several omics layers, which ultimately may result in a multi-omics panel allowing individualised UST therapy.

Methods : Inflamed colonic (n=25) and ileal (n=22) biopsies were retrieved prior to first UST administration in patients with active CD, in addition to sorted circulating CD14+ monocytes and CD4+ T-cells (n=39). RNA was extracted from both lysed biopsies and sorted cells, and RNA sequencing performed. Proteomic analysis was performed on baseline serum samples (n=86) using OLINK Proseek inflammation. Genotyping data was generated using ImmunoChip (n=38).

The genetic risk burden was determined for every patient using the SNPs which overlap with genes encoding functional proteins or RNAs. The 6 above-described layers of omics data were integrated and analysed using Multi-Omics Factor Analysis (MOFA). The strongest omic layers in terms of variance contribution to the latent factors explaining endoscopic response ($\geq 50\%$ in SES-CD by w24) were identified. Dimensionality reduction and feature extraction from the strongest -omic layers were performed followed by predictive modelling on the top ranked features. Cross-validation using distinct test and training sets was performed for the ensemble and individual classifiers, as an internal validation to avoid over-fitting.

Results : MOFA identified 19 latent factors (LF, minimum explained variance 2%), with 3 LFs correlating with endoscopic response at w24 ($r=-0.24$, $r=0.27$, $r=-0.25$; $p=0.03$, $p=0.01$, $p=0.02$ respectively). The genomic and CD14 transcriptomic layers contributed significantly to the prediction of endoscopic response. Predictive modelling based on the results of the most dominant omic layers revealed a 10-feature panel predicting endoscopic response at w24 with an accuracy of 98%. In contrast, classification performance based on 10 randomly selected features resulted in a drastic drop in accuracy (66%). Only 2 of the 10 features exhibited significant correlation with baseline faecal calprotectin, and 1 with CRP, suggesting that this panel is not a simple surrogate of baseline inflammation. From the genetic risk burden, we identified a 15-gene panel which could classify (accuracy 96.6%) the patients based on endoscopic response.

Conclusions : Through multi-omic data integration, we discovered pathways contributing to UST response, and identified a 10-feature transcriptomic and 15-feature genomic panel predicting endoscopic response to UST standard dosage. Further validation in larger and independent cohorts is warranted, as well as its UST specificity.

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GENETIC PREDISPOSITION AND THIOPURINE-INDUCED PANCREATITIS IN INFLAMMATORY BOWEL DISEASE PATIENTS. G. Burnet (1), N. de Suray (2), B. De Vroey (3), P. Hoang (4), J. Coche (5), M. Denis (1), J. Gala (6), O. Dewit (1) / [1] Clin universitaires St-Luc, UCL, Brussels, Belgium, Gastroenterology, [2] Grand Hopital de Charleroi, Charleroi, Belgium, Gastroenterology, [3] Hôpital de Jolimont, Haine-Saint-Paul, Belgium, Gastroenterology, [4] Clinique Sainte-Elisabeth, Namur, Belgium, Gastroenterology, [5] Clinique Saint-Pierre, Ottignies, Belgium, Gastroenterology, [6] Institut de Recherche Expérimentale et Clinique (IREC), Catholic University of Louvain (UCL), Belgium, Centre de Technologies Moléculaires Appliquées.

Introduction : Inflammatory bowel diseases (IBD), ulcerative colitis (UC) and Crohn's disease (CD), are chronic conditions leading to gastrointestinal tract inflammation and, ultimately, to tissue damage. Thiopurines (Azathioprine and 6-Mercaptopurine), remain an important treatment in both CD and UC. Unfortunately, they are responsible for side effects such as acute pancreatitis (AP) in 3 to 7% of patients. The underlying mechanism of this dose-independent immune-mediated allergic reaction is still unknown but genetic variability of enzymes intervening in thiopurine metabolism is known to influence adverse events linked to thiopurines. Results for inosine triphosphate pyrophosphatase (ITPA) are controversial. However, recent studies on HLA polymorphism demonstrated a significant link between single nucleotide polymorphism (SNP) rs2647087 and thiopurine-induced pancreatitis (TIP).

Aim : In this retrospective study, we wanted to evaluate if a supposed genetic predisposition could be demonstrated in our cohort of IBD patients who developed AP induced by thiopurines. This could indeed have future usefulness in screening IBD patients before starting thiopurines as it is actually the case for TPMT polymorphism, a strong predictor of bone marrow toxicity.

Methods : Out of 59 patients from five Belgian hospitals with a history of TIP, 42 met the eligibility criteria for AP linked to thiopurine with a positive temporal relationship (<4 weeks after thiopurine exposure) and exclusion of other causes of AP. A fully custom PCR amplicon-based target enrichment kit was developed based on the TruSeq Custom amplicon (TSCA) technology from Illumina (Illumina, San Diego, CA, U.S.A.). The design of the kit targeted ITPA, HLA-DQA1-HLA-DRB1, but also ABCC4, TPMT, MTHFR and GSTM1, known to intervene in thiopurine metabolism.

Results : Our cohort showed high rates of known risk factors for TIP such as CD (88.1%), women (73.8%) and smoking habits (50%). AP were mild or moderate and no early or late complication regarding AP was reported. Hospitalisation rate was 42.9% with a median stay of 6.1+/-5.43 days. No significant link between ITPA, ABCC4, TPMT, MTHFR, GSTM1 polymorphism and TIP could be found. However, in this cohort, SNP rs2647087 located on HLA-DQA1-HLA-DRB1, was found in high proportions (Allele frequency (AF)=0.476). These results are similar to a previous study of 172 TIP and 2035 thiopurine-tolerant controls (Heap et al., Nat. Gen., 2014) where an AF of 0.48-0.49 was found and to a smaller study of 13 cases and 360 controls (AF 0.69) (Wilson et al., Aliment Pharmacol Ther., 2018). Both studies demonstrated a significant link between this SNP and TIP with OR=2.59, $p=2 \times 10^{-16}$ (Heap et al.) respectively with OR=15.83, $p=0.0001$ (Wilson et al.).

Conclusions : TIP is a serious adverse event with important rate and duration of hospitalisation. Prevalence for HLA variant rs2647087 in this TIP cohort is significantly high. Results are similar than in previous studies where heterozygous and homozygous variants experienced a significant increased risk of TIP. Genotyping rs2647087 could be implemented in daily practice when discussing treatment options. Together with TPMT testing, it could be an interesting tool for guiding the physician and the patient in deciding whether or not it is appropriate to initiate thiopurine therapy. No association between ITPA polymorphism and TIP was observed.

UPREGULATION OF IL17-RELATED PATHWAYS IN AFFECTED COLON FROM ULCERATIVE COLITIS COMPARED TO CROHN'S DISEASE. S. Verstockt (1), F. Verdonck (1), B. Verstockt (2), E. Glorius (3), M. De Decker (4), V. Ballet (5), G. Van Assche (5), D. Laukens (3), M. Ferrante (2), F. Mana (4), M. De Vos (3), S. Vermeire (2), I. Cleynen (1) / [1] University of Leuven, Leuven, Belgium, Human Genetics, [2] University of Leuven, Leuven, Belgium, Translational Research Center for GastroIntestinal Disorders (TARGID), Department of Chronic Diseases, Metabolism and Ageing (CHROMETA), [3] University Hospital Gent, Gent, Belgium, Department of Gastroenterology, [4] University Hospitals Brussels, Belgium, Department of Gastroenterology, [5] University Hospitals Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction : Crohn's disease (CD) and ulcerative colitis (UC) can both affect the large intestine but harbour key differences in the type of inflammation. The underlying molecular differences might be important for guidance of therapeutic decisions.

Aim : We aimed to elucidate the molecular dysregulation in inflamed colonic biopsies from CD and UC patients at the time of diagnosis.

Methods : Patients naïve for biologicals and immunosuppressives, and without previous IBD-related surgery were prospectively included within 6 months after diagnosis, across three Belgian IBD centres (PANTHER study B322201627472/S57662). We collected serum and inflamed colonic biopsies from 52 patients: 31 CD (median age 25.1 (16.2-62.8) years; 65% male; 8 L2,23 L3) and 21 UC (age 29.3 (16.7-76.9) yrs; 43% male; 10 E2,11 E3). RNA was extracted from biopsies, and single-end RNA sequencing performed. Differential gene expression (fold change >2, adjusted p (adj. p) <0.05) and co-expression networks (adj. p ≤0.1) were analysed using DESeq2 and WGCNA (R), respectively. A panel of 91 serological inflammatory proteins (OLINK) was tested for correlation with the co-expression clusters.

Results : We found 336 (223 up, 113 down) differentially expressed genes between UC and CD, and 21 co-expression clusters. Four clusters were upregulated in UC, 3 in CD, the others did not show a difference between CD and UC. Genes within UC-upregulated clusters (I to IV) were mainly involved in (a) granulocyte adhesion/diapedesis, and in the role of IL-17 in psoriasis. CD-upregulated clusters (V to VII) were enriched for mitochondrial dysfunction and sirtuin signalling. Three clusters significantly correlated with serological marker levels: IL-6 with CD/UC cluster VIII, CDCP1 with CD/UC cluster IX, and IL-17A with UC cluster I (r=0.57, adj. p=0.10). The latter cluster was enriched for protein ubiquitination, which is known to be regulated by IL-17A. Of note, IL-17A serum levels were higher in UC than in CD (p<0.001), while IL-6 and CDCP1 were similar, which fits with the found correlations. Moreover, IL-17A tended to be positively correlated with UC-specific clusters II (r=0.52, adj. p=0.16) and III (r=0.54, adj.p= 0.12), with cluster II containing IL-17A and IL-23A, both significantly increased in UC compared to CD.

Conclusions : In treatment-naïve newly diagnosed CD and UC patients, we found both common and distinct gene expression profiles, such as an upregulation of IL-17 related pathways specifically in UC. Higher expression of these IL-17 pathways at mucosal level correlated with higher serological IL-17A. These differences potentially affect novel drug target identification and therapeutic decision-making, and emphasize the need for additional studies on the role and potential blockade of IL-23/IL-17 pathways in UC.

MOLECULAR CHANGES IN NON-INFLAMED TERMINAL ILEUM IN PATIENTS WITH ULCERATIVE COLITIS. H. Lee (1), M. Vancamelbeke (2), S. Verstockt (1), B. Verstockt (2), G. Van Assche (2), M. Ferrante (2), S. Vermeire (2), I. Cleynen (1) / [1] Laboratory for Complex Genetics, KU Leuven, Belgium, Department of Human Genetics, [2] Translational Research Center for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Department Chronic Diseases, Metabolism & Ageing (CHROMETA).

Introduction : Ulcerative colitis (UC) is a chronic inflammatory disease of the intestine, typically confined to the mucosal layer of the colon. Small intestinal dysfunction has, however, been described in patients with UC, although the underlying mechanisms of these alterations in apparently intact ileum are currently unknown.

Aim : We here evaluated molecular changes and biological networks in non-inflamed terminal ileum in UC, and their association with colonic inflammation.

Methods : Terminal ileum biopsies were obtained during endoscopy from 36 patients with UC (7 active (Mayo endoscopic subscore ≥2) and 29 inactive) and 16 healthy controls. Subjects with endoscopic or histological (backwash) ileitis were not included. Single-end RNA sequencing was performed using Illumina HiSeq4000. Gene expression differences were analysed using DESeq2, and corrected for age and gender. Weighted gene co-expression network analysis (WGCNA) was performed to find biological networks of genes that correlate with UC activity. Pathways and upstream regulators were identified using IPA.

Results : When we compared ileal expression levels of active UC (71% male; median age 52 years; disease extent at endoscopy: n=4 E2, n=3 E3) with controls (44% male, median age 57 years), we found 20 differentially expressed (adj. $p \leq 0.05$ and fold change (FC) ≥ 2) genes, with DUOXA2 being the most significant (FC=4.9, adj. $p=0.009$). The 20 genes were involved in free radical scavenging, molecular transport, cell-to-cell signalling, and cellular proliferation. Cytokines IL1A, IFNG, and TNF were predicted as upstream regulators. Comparison of inactive UC (59% male; median age 52 years; previous maximal disease extent: n=3 E1, n=11 E2, n=13 E3) with controls only found 2 dysregulated genes (CEBPD and REG1B). REG1B was also one of the 20 dysregulated genes in active UC (active UC: FC=4.1, adj. $p=0.02$; inactive UC: FC=2.7, adj. $p=0.04$). WGCNA analysis found 38 co-expression modules, 3 of which were positively correlated (adj. $p \leq 0.2$) with active UC versus controls. The genes enclosed in these clusters were mainly involved in immune functions (e.g. interferon and cytokine signalling, and antigen presentation). Importantly, this correlation seemed driven by active disease with extensive colitis (E3) at time of biopsy only, as no significant correlation was observed with active E2 disease versus controls. One module was positively correlated with inactive UC (enriched for genes involved in mitochondrial translation), and one was negatively correlated (enriched in signal regulatory protein (SIRP) family interactions and NF- κ B activation genes). Both clusters were correlated irrespective of previous maximal disease extent.

Conclusions : Our transcriptome analysis identified significant alterations in non-inflamed ileum of UC patients, depending on extent of colonic inflammation. Ileal changes in active extensive UC are mainly related to immune function, but the causal and temporal relationship with colonic inflammation is unclear. Ileal changes in inactive UC on the other hand seem to be functioning to maintain the intestinal barrier with increased mitochondrial functions and dampened immune functions.

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HEPATOCTE GROWTH FACTOR AND MET IN ULCERATIVE COLITIS, NOVEL DRUG TARGETS IMPAIRING NEUTROPHIL RECRUITMENT? M. Stakenborg (1), B. Verstockt (1), E. Meroni (1), W. Wollants (1), M. Ferrante (2), M. Di Matteo (3), M. Mazzone (3), G. Boeckxstaens (1), S. Vermeire (2), G. Matteoli (1) / [1] KU Leuven, Belgium, TARGID, [2] University Hospitals Leuven, Belgium, Gastroenterology, [3] KU Leuven, Belgium, Lab of Tumor Inflammation and Angiogenesis.

Introduction : Neutrophils are crucial in the maintenance of intestinal homeostasis and inflammation. However, during chronic inflammatory conditions, like Inflammatory Bowel Disease (IBD), the intestinal immune system responds inaccurately resulting in excessive neutrophil infiltration and tissue damage.

Aim : Since MET is required for neutrophil chemoattraction and cytotoxicity in response to its ligand hepatocyte growth factor (HGF), we aim to identify the function of the HGF-MET axis in neutrophils during intestinal inflammation in a mouse model of colitis and in patients with ulcerative colitis (UC) and healthy controls (HC).

Methods : Acute colitis was induced in wild type mice (WT, C57BL/6) and mice with MET deficiency in neutrophils (MRP8-Cre MET-LoxP (KO)) by 2,5% dextran sodium sulfate (DSS). Disease progression was assessed via a standardized disease activity index (DAI) including body weight loss, stool consistency and blood in the feces. Immune cell infiltration in the colon was assessed by flow cytometry. Serum of HC (n=30) and inflamed UC patients (n=110) was collected, prior to the start of anti-TNF therapy, and at endoscopic reassessment (8-14 weeks after treatment initiation). Endoscopic remission was defined as a Mayo endoscopic sub-score ≤ 1 . HGF was measured using electrochemiluminescence (MSD). Additionally, RNA sequencing (Illumina HiSeq4000) was performed on inflamed colonic biopsies in a subset of 24 UC patients and 11 HC.

Results : HGF was upregulated both during the acute phase of dextran sodium sulphate (DSS) colitis and in patients with active ulcerative colitis (UC). In addition, Met deletion in mouse neutrophils during acute DSS colitis improved disease severity together with reduced immune cell infiltration, in particular neutrophils, eosinophils and macrophages. Moreover, the percentage of FoxP3+ T regulatory cells was increased in KO mice compared to their WT counterparts, pointing towards a return to homeostasis in the KO colon. Strikingly, analysis of CD4+ T cells showed a predominant decrease of the percentage IL17A+ Th17 and IL17A+ IFN γ + Th1-like Th17 in KO mice compared to WT mice, while no differences were observed in the percentage of IFN γ + Th1 cells. Serum HGF was significantly upregulated in active UC patients compared to HC ($p=0.001$, fold change FC 1.5). Similarly, colonic HGF and MET expression were significantly upregulated compared to healthy individuals ($p=3.2E10^{-6}$, FC 5.8; $p=0.0007$, FC 1.8 respectively). Serum HGF correlated significantly with tissue MET expression ($r=0.47$, $p=0.03$), but not with tissue HGF expression ($r=0.23$, $p=0.30$). Patients with a Mayo endoscopic sub-score of 3 had significantly higher serum HGF levels as compared to patients with a sub-score of 2 prior to therapy initiation ($p=0.007$, FC 1.2). Additionally, serum HGF levels correlated significantly with C-reactive protein ($r=0.44$, $p=9.5E10^{-12}$) and absolute neutrophils counts ($r=0.62$, $p=2.2E10^{-16}$). However, baseline HGF was not predictive for anti-TNF induced endoscopic remission later on ($p=0.39$). After anti-TNF administration, HGF levels overall decreased ($p=1.2E10^{-7}$) and reached values similar to HC in case of endoscopic remission ($p=0.35$). At the time of endoscopic assessment, patients with endoscopic remission had significantly lower HGF levels than those without ($p=0.0003$, FC 0.72).

Conclusions : Colonic and serum HGF levels are significantly upregulated in active UC patients, with restoration towards physiological levels in patients with anti-TNF induced endoscopic remission. As murine findings suggest that absence of MET in neutrophils reduces intestinal inflammation, targeting MET could be considered as a novel therapeutic approach in UC therapy.

- I07 -

ORGANOIDS DERIVED OF INFLAMMATORY INTESTINAL BIOPSIES IN ULCERATIVE COLITIS PATIENTS LOSE THEIR INFLAMMATORY TRANSCRIPTIONAL SIGNATURE OVER TIME. K. Arnauts (1), B. Verstockt (2), M. Vancamelbeke (2), S. Vermeire (2), C. Verfaillie (3), M. Ferrante (2) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing, [2] Translational Research Center for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism & Ageing, [3] Stem Cell Institute (SCIL), KU Leuven, Leuven, Belgium, Department of Development and Regeneration.

Introduction : Patient-derived intestinal organoids provide an excellent tool to unravel the multifactorial mechanisms underlying ulcerative colitis (UC). Organoids develop from stem cell-containing intestinal crypts and recapitulate many features of the source tissue. However, it remains unclear if organoids retain the inflammatory character of their origin. **Aim** : To address if organoids maintain the inflammatory character, we isolated crypts from both inflamed and non-inflamed regions of the colon, created organoids and compared the transcriptome of whole biopsies, crypts and ex vivo cultured organoids.

Methods : Fresh biopsies in both inflamed and non-inflamed segments were obtained during endoscopy from 8 patients with active UC (endoscopic Mayo sub-score of ≥ 2) with an accessible border of inflammation. Crypts were isolated from fresh biopsies and cultured as organoids for 4 weeks with weekly mechanical splitting. RNA was extracted from biopsies, crypts and 1- and 4-week old organoids. RNA sequencing was performed by Lexogen QuantSeq for Illumina. Differential gene expression and pathways were studied through DESeq2 and Ingenuity Pathway Analysis. All p-values are adjusted for multiple testing (False Discovery Rate).

Results : Biopsies and crypts from inflamed regions showed separate clustering on principal component analysis (PCA) and significantly higher activation of inflammatory pathways including antigen presentation ($p < 0.01$ and $p < 0.001$), interferon signalling ($p < 0.05$ and $p < 0.001$) and granulocyte adhesion (both $p < 0.001$) compared to biopsies and crypts of non-inflamed regions. However, organoids derived from inflamed crypts lost part of their inflammatory character after 1 week in culture. Several inflammatory markers (IFN- γ ($p = 0.01$), IL-1 β ($p < 0.001$), JAK1 ($p < 0.001$)) and pathways involved in antigen presentation ($p < 0.005$) and interferon signalling ($p < 0.001$) were significantly decreased after 1 week ex vivo culture compared to inflamed crypts. After 4 weeks in culture, organoids derived from inflamed and non-inflamed regions were indistinguishable in PCA clustering. Expression levels of inflammatory signalling pathways were not significantly different in organoids derived from inflamed and non-inflamed biopsies after 4 weeks in culture.

Conclusions : We conclude that organoids lose their inflammatory transcriptional signature, present in biopsies and isolated crypts, over time in culture. After 4 weeks in culture, organoids derived from inflamed and non-inflamed biopsies were no longer distinguishable. Therefore, it is not essential to obtain biopsies from inflamed regions to culture organoids from UC patients. We hypothesize that to mimic the inflammatory phenotype and create a physiological representative model, inflammatory components and/or immune cells should be added to the ex vivo culture system.

- I08 -

TREM1, THE FIRST ANTI-TNF SPECIFIC BIOMARKER GUIDING THERAPEUTIC DECISION. B. Verstockt (1), S. Verstockt (2), J. Dehairs (3), V. Ballet (4), H. Blevi (5), W. Wollants (5), C. Breynaert (6), G. Van Assche (5), S. Vermeire (5), M. Ferrante (5) / [1] Translational Research Center for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Department of Chronic Diseases, metabolism and ageing, [2] Laboratory for Complex Genetics, KU Leuven, Belgium, Department of Human Genetics, [3] Laboratory of Lipid Metabolism and Cancer, KU Leuven, Belgium, Department of Oncology, [4] University Hospitals Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology, [5] Translational Research Center for Gastrointestinal Disorders (TARGID), KU Leuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing, [6] Laboratory of Clinical Immunology, KU Leuven, Belgium, Department of Microbiology and Immunology.

Introduction : With the expanding therapeutic armamentarium for inflammatory bowel diseases (IBD), biomarkers predicting efficacy are urgently needed.

Aim : To predict outcome to anti-TNF therapy, we studied whole blood and mucosal expression of genes previously reported to predict outcome to anti-TNF therapy, and investigated if the signature was specific for these agents.

Methods : We prospectively included 35 (discovery) and 19 (validation) consecutive IBD patients with active disease (both Crohn's disease and ulcerative colitis) initiating anti-TNF therapy, as well as 22 patients initiating ustekinumab

and 51 patients initiating vedolizumab. Whole blood expression levels of OSM, TNF, TNFR2 and TREM1 (total and all individual transcripts separately) were measured prior to start of therapy using qPCR, and mucosal gene expression in inflamed biopsies using RNA-sequencing. Endoscopic remission was defined as an SES-CD \leq 2 at week 24 for Crohn's disease and a Mayo endoscopic sub-score \leq 1 at week 8-14 for ulcerative colitis.

Results : Baseline whole blood TREM1 expression was significantly downregulated in future anti-TNF healers ($p<0.001$, both discovery and validation cohort). Receiver operator characteristic statistics showed an area under the curve (AUC) of 0.78 ($p=0.001$), resulting in post-test probabilities of 77.1% and 90.0% for endoscopic remission and non-remission, respectively. A similar accuracy could be observed in mucosal TREM1 expression (AUC 0.77, $p=0.003$), which outperformed the accuracy of serum TREM1 at the protein level (AUC 0.58, $p=0.31$). Whole blood TREM1 expression did not significantly correlate with CRP (spearman = -0.08, $p=0.38$), faecal calprotectin (spearman = -0.06, $p=0.64$) or serum TNF (spearman = -0.15, $p=0.63$). OSM, TNF and TNFR2 were not differentially expressed in whole blood ($p=0.09$, $p=0.13$, $p=0.24$ respectively), whereas they were at the mucosal level ($p=0.007$, $p=0.02$, $p=0.008$ respectively). The whole blood TREM1 predictive signal was anti-TNF specific, as no changes in expression were seen in ustekinumab and vedolizumab treated patients, neither in whole blood ($p=0.82$, $p=0.53$ respectively), nor in tissue ($p=0.24$, $p=0.10$, respectively).

Conclusions : We identified and validated low TREM-1 as a specific biomarker for anti-TNF induced endoscopic remission. These results can aid in the selection of therapy in biological-naïve patients, but should be confirmed in a randomized trial prior to translation into daily clinical practice.

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VEDOLIZUMAB-INDUCED ENDOSCOPIC REMISSION IN ANTI-TNF EXPOSED AND ANTI-TNF NAÏVE IBD PATIENTS: A LARGE SINGLE CENTRE EXPERIENCE. B. Verstockt (1), E. Mertens (1), A. Outtier (1), G. Van Assche (1), S. Vermeire (1), M. Ferrante (1) / [1] University Hospitals Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction : Vedolizumab (VDZ), a gut-focused biological agent targeting alpha4beta7 and hence preventing leukocyte trafficking into the intestinal wall, has demonstrated efficacy and safety in patients with Crohn's disease (CD) and ulcerative colitis (UC). Real-life endoscopic remission data are still very limited, especially in anti-TNF naïve patients.

Aim : The present study compared VDZ-induced endoscopic outcome in anti-TNF naïve and exposed patients.

Methods : We retrospectively assessed the medical charts of all IBD patients ($n=408$) who initiated VDZ therapy at our tertiary referral centre after the pivotal clinical trials, from January 2015 till April 2018, and who had a minimal follow-up of 6 months at our centre. Patients with an ostomy ($n=11$) or ileoanal pouch ($n=20$), as well patients without active disease ($n=41$) at start were excluded from the analysis. All patients received VDZ 300mg IV at week 0,2,6 and q8w thereafter. CD patients received an additional dosage at week 10. Endoscopic remission was defined as a Mayo endoscopic subscore \leq 1 at week 14 (as per national reimbursement criteria) for UC, and absence of ulcerations at month 6 for CD. All endoscopies were performed by the same 3 IBD staff members. Non-responder imputation was applied for patients discontinuing VDZ prior to the endoscopic endpoint.

Results : Of the 336 patients included (53.3% CD, 46.7% UC), 80.1% had been exposed to at least one anti-TNF agent (37.2% one, 39.0% two, 3.9% three anti-TNF agents), with endoscopic outcome available in 96.1% of patients. After a median (IQR) of 14.0 (13.6-14.6) weeks, 56.4% of UC patients achieved endoscopic remission, whereas 41.9% of CD patients experienced endoscopic remission after 22.1 (21.6-25.0) weeks (L2 (62.5%) vs L1+L3 (38.5%), $p=0.03$). No difference in disease duration could be found between remitters and non-remitters ($p=0.70$). Significantly more anti-TNF naïve vs anti-TNF exposed patients achieved endoscopic remission [69.2% vs 44.0%, OR 2.9 (95% CI 1.6-5.2), $p=0.0003$], which was seen for both CD [61.5% vs 38.3%, 2.6 (1.1-6.1), $p=0.03$] and UC [73.7% vs 51.3%, 2.7 (1.2-6.0), $p=0.02$]. No difference in remission rates was observed between patients failing 1 vs \geq 2 anti-TNF agents ($p=0.26$). Similarly, no effect of corticosteroids or immunomodulators during induction could be observed with regard to endoscopic remission ($p=0.61$, $p=0.86$ respectively).

Conclusions : This is the biggest, real-life, single centre cohort study confirming that VDZ can induce endoscopic remission in both CD and UC patients, without any effect of concomitant therapy during induction. Although anti-TNF naïve patients had a significantly better outcome, 44% of anti-TNF exposed patients did achieve endoscopic remission.

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PREGNANCY OUTCOMES IN IBD PATIENTS TREATED WITH VEDOLIZUMAB, ANTI-TNF OR CONVENTIONAL THERAPY. A. Moens (1), C. van der Woude (2), M. Julsgaard (3), S. Sebastian (4), N. Arebi (5), M. Alzinaty (5), E. Humblet (6), K. Kok (7), J. Sheridan (8), C. Gilletta De Saint-Joseph (9), S. Nancey (10), J. Rahier (11), P. Bossuyt (12), A. Cremer (13), S. Dewit (14), C. Eriksson (15), F. Hoentjen (16), T. Krause (17), E. Louis (18), E. Macken (19), Z. Milenkovic (20), J. Nijs (21), A. Posen (22), A. Van Hootegem (23), W. Van Moerkercke (24), S.

Vermeire (1), A. Bar-Gil Shitrit (25), M. Ferrante (1) / [1] UZ Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] Erasmus Medical Center, Rotterdam, The Netherlands, Department of Gastroenterology and Hepatology, [3] Aarhus University Hospital, Aarhus, Denmark, Aarhus, Denmark, Department of Hepatology and Gastroenterology, [4] Hull & East Yorkshire NHS Trust, Hull, UK, Hull, United Kingdom (the), IBD Unit, [5] St. Marks Hospital, London, United Kingdom (the), Department of Gastroenterology, [6] Ziekenhuis Oost Limburg (ZOL), Genk, Belgium, Department of Gastroenterology and Hepatology, [7] Barts Health NHS Trust, London, United Kingdom (the), Department of Gastroenterology, [8] St. Vincent's University Hospital, Dublin, Ireland, Department of Gastroenterology, [9] Hôpital Rangueil, Toulouse, France, Department of Gastroenterology, [10] CHU Lyon, Lyon, France, Department of Gastroenterology, [11] CHU UCL Namur, Yvoir, Belgium, Department of Gastroenterology, [12] Imeldaziekenhuis, , Belgium, Department of Gastroenterology, [13] Erasme Hospital, Brussels, Belgium, Department of Gastroenterology, [14] Mariaziekenhuis Noord-Limburg, Overpelt, Belgium, Department of Gastroenterology, [15] Faculty of Medicine and Health Orebro University, Orebro, Sweden, Department of Gastroenterology, [16] Radboud UMC, Nijmegen, The Netherlands, Department of Gastroenterology, [17] Opernstrasse, Kassel, Germany, Department of Gastroenterology, [18] CHU Liege, Liège, Belgium, Department of Gastroenterology, [19] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Department of Gastroenterology, [20] Military Medical Academy Belgrade, Belgrade, Serbia, Department of Gastroenterology, [21] Sint-Trudo ziekenhuis, Sint-Truiden, Sint-Truiden, Belgium, Department of Gastroenterology, [22] AZ Vesalius Tongeren, Tongeren, Belgium, Department of Gastroenterology, [23] KLINA, Brasschaat, Belgium, Department of Gastroenterology, [24] AZ Groeninge, Kortrijk, Belgium, Department of Gastroenterology, [25] Shaare Zedek Medical Center, Hebrew University Jerusalem, Jerusalem, Israel, Digestive diseases institute.

Introduction : Women with inflammatory bowel diseases (IBD) often receive biologicals during pregnancy to maintain disease remission prior to conception and throughout pregnancy. However, data on vedolizumab exposed pregnancies (VDZE) are scarce.

Aim : The aim of this study was to assess outcomes of VDZE pregnancies in IBD patients and to compare these results to outcomes of anti-TNF exposed (TNFE) or immunomodulatory and biologic unexposed (IBU) pregnancies.

Methods : This retrospective multicentre observational study assessed outcomes of VDZE pregnancies in IBD patients (group A). European gastroenterologists were asked to report all VDZE pregnancies. Details of underlying IBD, pre- and postnatal outcomes were collected through a case report form. Results were compared to TNFE (group B) or IBU (group C) pregnancies. The control groups were prospectively enrolled in two different centres with a specialized IBD preconception and pregnancy clinic. Nominal data were reported as percentages and compared using Fisher's exact test, while continuous data were expressed as medians with interquartile ranges (IQR) and compared using Mann-Whitney U test. A p-value <0.05 was regarded as statistically significant.

Results : Results Group A included 86 pregnancies in 81 women [53% Crohn's disease (CD), 70 live births] from 31 centres in 11 countries. The groups were comparable regarding baseline characteristics, though group A included more women with ileocolonic CD and perianal involvement. In addition, at conception 35% of these women had active disease, 17% were on steroids and 20% on immunomodulators. Also, 54% already failed two previous biologicals. Group B and C included 186 pregnancies in 155 women and 185 pregnancies in 164 women (83% vs. 55% CD, 162 vs. 163 live births). Controls had less active disease at conception (B: 16%, C: 24%) and fewer were taking steroids (B: 8%, C: 14%). Miscarriages were more commonly seen in group A than B (16% vs. 13%, p=0.46) and C (16% vs. 8%, p=0.03). However, after excluding patients with reported active disease in pregnancy, the number of miscarriages was similar in group A compared to B (14% vs. 14%, p=1.0) and C (14% vs. 12%, p=0.80). In live-born infants, median gestational age and birth weight were comparable between groups A and B [39 (IQR 38-40) vs. 39 (IQR 38-40) weeks, p=0.17; 3298 (IQR 2868-3600) vs. 3215 (IQR 2835-3555) gram, p=0.45] as well as A and C [39 (IQR 38-40) vs. 39 (IQR 38-40) weeks, p=0.71; 3298 (IQR 2868-3600) vs. 3237 (IQR 2867-3600) gram, p=0.39]. Also, median Apgar score at birth (9) was numerically equal in all groups. The number of premature born children was not significantly different in group A compared to B (16% vs. 9%, p=0.16), nor was the amount of reported congenital anomalies (4% vs. 2%, p=0.43). The percentages of breastfed children were similar in all groups [A: 61%, B: 60%, C: 64%, p=0.89 and p=0.68]. During the first year of life, no malignancies were reported and the infants' infection risk was comparable between groups (A: 7%, B: 10%, C: 12%, p=0.56 and p=0.38).

Conclusions : Conclusion VDZE pregnancies were associated with more miscarriages, yet active disease in pregnancy rather than drug effect seems to be the driver of this adverse pregnancy outcome, since no significant difference is observed after exclusion of patients with reported active disease. Still larger prospective studies are needed for confirmation.

Vermeire (2) / [1] Hopital Erasme, ULB, Belgium, Department of Gastroenterology, [2] University Hospitals Leuven, Belgium, Department of Gastroenterology and Hepatology, [3] KU Leuven, Belgium, Department of Pharmaceutical and Pharmacological Sciences, [4] Centre Hospitalier Universitaire Sart-Tilman, ULG, Belgium, Department of Gastroenterology and Hepatology, [5] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Department of Gastroenterology, [6] Universitair ziekenhuis Gent, Belgium, Department of Gastroenterology, [7] AZ Groeninge Hospital, Kortrijk, Belgium, Department of Gastroenterology, [8] Centre Hospitalier Universitaire Mont-Godinne, Belgium, Department of Gastroenterology, [9] Imeldaziekenhuis, Bonheiden, Belgium, Department of Gastroenterology, [10] Ziekenhuis Netwerk Antwerpen, Belgium, Department of Gastroenterology, [11] Ziekenhuis Oost-Limburg - Campus Sint-Jan, Belgium, Department of Gastroenterology, [12] GZA Sint-Vincentius ziekenhuis, Antwerpen, Belgium, Department of Gastroenterology, [13] Algemeen Ziekenhuis Sint-Lucas, Gent, Belgium, Department of Gastroenterology, [14] Algemeen Ziekenhuis Sint-Lucas, Brugge, Belgium, Department of Gastroenterology, [15] Centre Hospitalier Universitaire Sart-Tilman, ULG, Belgium, Department of Gastroenterology, [16] Hôpital Erasme, ULB, Belgium, Department of Gastroenterology, [17] AZ Delta, Belgium, Department of Gastroenterology.

Introduction : Ustekinumab (UST) was recently approved in Belgium for moderate to severe Crohn's disease (CD). Long-term real-life data are currently scarce, especially in refractory populations.

Aim : To report real world long-term efficacy data in a Belgian cohort (14 centres) with prior exposure to both anti-TNF and vedolizumab.

Methods : We collected data in patients initiating UST therapy between 09/2016 and 09/2017 Patients received intravenous (IV) UST 6mg/kg at baseline, with 90 mg subcutaneously thereafter every 8 weeks. The primary endpoints, clinical response and remission at one year, were defined as a reduction in Harvey Bradshaw Index (HBI) of ≥ 3 and a HBI ≤ 4 , respectively. Biological response was defined as 50% drop in C-reactive protein (CRP) and/or CRP $< 5\text{mg/L}$ and biological remission as CRP $< 5\text{mg/L}$, if CRP $> 5\text{mg/l}$ at baseline. Primary nonresponse was defined as drug stop due to absence of clinical improvement before week 8 while loss of response as drug stop due to secondary loss of response after initial response to the drug. Data were analyzed in an intention-to-treat manner

Results : 163 CD patients constituted the study cohort. The majority of CD patients had an ileo-colonic involvement and 55.3 % had a complicated behaviour (B2/B3). An history of peri-anal disease was found in 39.3%, and 61.9% of patients had a surgery related to CD. All patients except one due to a neoplastic contraindication were exposed to one anti-TNF. 77.3% and 71.2% of the cohort were previously exposed to two anti-TNF, and two anti-TNF and vedolizumab respectively. At baseline, concomitant steroids use was used in 43.7% of patients. Baseline CRP was available for 150 patients of which 110 (73.3%) had CRP $> 5\text{mg/l}$. Baseline HBI was available for 153 patients of which 142 (93%) had HBI > 4 . Data at one year were available for all but 8 patients due to loss of follow-up. 11 patients with HBI ≤ 4 at baseline were excluded. By one year of follow-up, 42.1% experienced a clinical response including 35.7% of patients with clinical remission. 38.8% and 24.3% of the population obtained a steroid-free clinical response and remission, respectively. Treatment intensification (new IV infusion and/or q4w) was reported in 6.6% of patients. UST was discontinued in 35.5% of patients after one year. Reasons for UST withdrawal were primary nonresponse (n=3), intense arthralgia (n=1), loss of response (n=47) and patient decision (n=4). CRP significantly decreased from baseline (16.1 mg/L, IQR [10.6-28.8]) to 6.6 mg/L at one year (IQR [6.6-15.1], $p < 0.0001$). At week 52, a 50% drop in CRP was observed in 33.6% and 25.4% achieved a biological remission. Eleven patients (6.7%) of patients experienced side effects, including one patient who discontinued therapy due to intense arthralgia.

Conclusions : This real-life cohort study confirms the clinical efficacy of ustekinumab at one year even in a population of highly refractory CD patients.

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TARGETING ENDOSCOPIC OUTCOMES THROUGH COMBINED PHARMACOKINETIC AND PHARMACODYNAMIC MONITORING OF INFlixIMAB THERAPY IN PATIENTS WITH CROHN'S DISEASE. E. Dreesen (1), F. Baert (2), D. Laharie (3), P. Bossuyt (4), Y. Bouhnik (5), A. Buisson (6), G. Lambrecht (7), E. Louis (8), B. Oldenburg (9), B. Pariente (10), M. Pierik (11), C. van der Woude (12), G. D'haens (13), S. Vermeire (14), A. Gils (1) / [1] University of Leuven, Leuven, Belgium, Department of Pharmaceutical and Pharmacological Sciences, [2] AZ Delta, Roeselare, Belgium, Department of Gastroenterology, [3] Hôpital Haut-Lévêque, Bordeaux, France, Service d'Hépatogastroentérologie et Oncologie Digestive, [4] Imelda Hospital, Bonheiden, Belgium, IBD Clinic, [5] Beaujon Hospital, Clichy, France, Department of Gastroenterology, [6] Estaing University Hospital, Clermont-Ferrand, France, Department of Gastroenterology, [7] AZ Damiaan, Oostende, Belgium, Department of Gastroenterology, [8] University Hospital CHU of Liège, Liege, Belgium, Department of Gastroenterology, [9] University Medical Center Utrecht, The Netherlands, Department of Gastroenterology and Hepatology, [10] Hôpital Huriez, Lille, France, Department of Gastroenterology, [11] Maastricht University Medical Centre, Maastricht, The Netherlands, Department of Gastroenterology and Hepatology, [12] Erasmus Medical Center, Rotterdam, The Netherlands, Department of Gastroenterology and Hepatology, [13] Academic Medical Center, Amsterdam, The Netherlands, Department of Gastroenterology, [14] University Hospitals Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction : In the TAILORIX trial, infliximab trough concentrations >23.1 mg/L at week 2 and >10.0 mg/L at week 6 predicted endoscopic remission (Crohn's disease endoscopic index of severity <3) at week 12.[1] During maintenance therapy, no exposure-response relation was observed, but faecal calprotectin was significantly lower in patients achieving the endoscopic outcomes compared to patients who did not.[1]

Aim : To explore the value of combined pharmacokinetic and pharmacodynamic monitoring of infliximab dosing in patients with Crohn's disease.

Methods : A two-compartment population pharmacokinetic model was developed based on data from 1,329 samples from 116 patients in TAILORIX (NONMEM 7.4).[2]

Results : In line with the previously observed higher infliximab trough concentrations[1], also the estimated infliximab clearance during induction therapy was lower in patients achieving endoscopic remission at week 12 (-0.067 ± 0.020 L/d, $P = 0.001$), but this was not observed during maintenance therapy ($P > 0.05$). During maintenance therapy, an exposure-response relationship was observed only after dose escalation, with a trough concentration >10.8 mg/L after dose escalation predicting absence of ulceration at week 54 (sensitivity 96%, specificity 36%, positive predictive value 52%, negative predictive value 93%, positive likelihood ratio 1.50, negative likelihood ratio 0.11, area under the receiver-operating characteristic curve 0.69). However, this exposure-response relation only appeared after three infusions at the elevated dose. Furthermore, in patients with elevated faecal calprotectin (>250 mg/kg), a significant drop was observed right upon dose escalation, resulting in faecal calprotectin concentrations that were significantly lower in patients without ulcers compared to patients with ulcers ($P = 0.033$). Antibodies to IFX (ATI), measured using a drug-tolerant assay, increased the infliximab clearance with $\sim 48\%$, resulting in a reduction of the terminal half-life from 9.4 to 6.4 days. Still, infliximab was detectable in 70% of ATI+ samples. Study dropout was significantly higher in ATI+ patients ($P < 0.0001$). In addition, infliximab exposure reduced when albumin was lower and faecal calprotectin and fat free mass were higher.

Conclusions : We recommend proactive and reactive monitoring of faecal calprotectin during infliximab maintenance therapy, but when faecal calprotectin does not normalise upon dose escalation, the infliximab trough concentration provides information on the mechanism of failure and can thus guide clinical decision-making. Future prospective trials are needed to evaluate this proposed therapeutic drug monitoring algorithm. References: [1] Dreesen E, D'Haens G, Baert F, et al. DOP047 Infliximab exposure predicts superior endoscopic outcomes in patients with active Crohn's disease: pharmacokinetic-pharmacodynamic analysis of TAILORIX (weblink). [2] D'Haens G, Vermeire S, Lambrecht G, et al. Increasing Infliximab Dose Based on Symptoms, Biomarkers, and Serum Drug Concentrations Does Not Increase Clinical, Endoscopic, and Corticosteroid-Free Remission in Patients With Active Luminal Crohn's Disease. *Gastroenterology* 2018; 154:1343–1351.e1.

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A POPULATION PHARMACOKINETIC MODEL TO IMPROVE MUCOSAL HEALING UPON GOLIMUMAB INDUCTION THERAPY IN PATIENTS WITH ULCERATIVE COLITIS. W. Kantasiripitak (1), E. Dreesen (1), I. Detrez (1), S. Stefanovic (2), D. Drobne (2), S. Vermeire (3), M. Ferrante (3), A. Gils (1) / [1] KU Leuven, Belgium, Pharmaceutical and Pharmacological Sciences, [2] University Medical Centre Ljubljana, Ljubljana, Slovenia, Gastroenterology and Hepatology, [3] University Hospitals Leuven, Belgium, Gastroenterology and Hepatology.

Introduction : Golimumab is a human monoclonal anti-tumor necrosis factor (TNF)- α antibody for the treatment of patients with moderately to severely active ulcerative colitis. From the PURSUIT programme, it is known that golimumab trough concentrations above 2.5 mg/L at week 6 of the induction therapy are associated with clinical response in patients with ulcerative colitis. No trough concentration threshold has been established for mucosal healing (Mayo endoscopic sub-score ≥ 1). Better understanding of the golimumab exposure could improve treatment in the patients.

Aim : A population pharmacokinetic (popPK) model was employed to define exposure-response relationships and to improve attainment of a predefined trough concentration target.

Methods : Golimumab concentration-time data of 56 patients with ulcerative colitis (335 venepuncture and 296 dried blood spot samples) were obtained from two study centres (University Hospitals Leuven, Belgium and Ljubljana University Medical Centre, Slovenia). A popPK model was developed using NONMEM (version 7.4). The effects of potential covariates were evaluated. Exposure during golimumab induction therapy was linked to mucosal healing at week 14. Trough concentration threshold for the outcome was then assessed with receiver operating characteristics (ROC) curve analysis and density plot.

Results : A two-compartment popPK model with linear absorption and elimination showed good predictive performance. The estimated popPK parameters (typical value [%relative standard error]) were absorption rate constant k_a (0.511 day⁻¹ [8%]), apparent clearance CL/F (0.407 L/day [6%]), volume of distribution in the central compartment V_c/F (9.16 L [5%]) and peripheral compartment V_p/F (3.21 L [22%]) and intercompartmental clearance Q/F (0.464 L/day [13%]). Antibodies to golimumab and higher alkaline phosphatase increased golimumab CL/F, while prior biological use was associated with a larger V_p/F , all predicting lower golimumab exposure. Still, 48% and 147% of the interindividual variability on CL/F and V_p/F remained unexplained. A total of 14/40 patients (35%, 16/56 no endoscopy data available)

achieved mucosal healing after golimumab induction therapy. These patients had significantly higher model predicted golimumab trough concentration at week 6 (median 7.6 mg/L, interquartile range [5.8 – 8.0]) compared to patients not achieving mucosal healing (4.7 [3.3 – 6.8]; $P=0.005$). A threshold of 7.4 mg/L (92% sensitivity, 57% specificity, 80% negative predictive value, 80% positive predictive value, positive likelihood ratio 2.14, negative likelihood ratio 0.14, area under the ROC curve [95% confidence interval] 0.77 [0.60-0.93]) was established from the predicted golimumab trough concentration at week 6. Only 10/40 (25%) patients achieved the proposed 7.4 mg/L target at week 6. In addition, the estimated area under the golimumab concentration-time curve from week 0 to week 6 was higher when mucosal healing was achieved ($P=0.010$).

Conclusions : With the currently approved induction dosing of golimumab, a substantial proportion of patients are underexposure. This popPK model shows good predictive performance and may be implemented in a therapeutic drug monitoring software tool to allow better targeting of the here established exposure target in individual patients. Bayesian updating of individuals' pharmacokinetics parameters using early dried blood spot samples is recommended given the remaining large unexplained interindividual variability.

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SIGNIFICANT REDUCTION OF ADMISSION TIME AT THE IBD INFUSION UNIT BY AN E-HEALTH PRE-ADMISSION ASSESSMENT AND ORDER SYSTEM FOR INTRAVENOUS THERAPY. E. Hoefkens (1), L. Pouillon (1), V. Verheyen (2), M. Bronswijk (1), A. Van Olmen (1), S. Van Dessel (3), N. Siborgs (4), P. Bossuyt (1) / [1] Imelda Hospital, Bonheiden, Belgium, Department of gastroenterology, [2] Imelda Hospital, Bonheiden, Belgium, Hospital Pharmacy, [3] Imelda Hospital, Bonheiden, Belgium, IBD infusion unit, [4] Imelda Hospital, Bonheiden, Belgium, IT department.

Introduction : The regularly administration of intravenous (IV) therapy negatively impacts on the work productivity and social functioning of patients with inflammatory bowel disease (IBD). The advent of new IV therapies leads to an increased workload at the IBD infusion unit and pharmacy, demanding a more efficient organisation. E-health tools may optimize patient time consumption and workflow at the IBD infusion unit and pharmacy.

Aim : Our aim was to assess the feasibility, adoption and impact on time consumption of an automatic online pre-admission assessment and order system for patients with IBD.

Methods : We developed an online platform, directly linked to the electronic agenda of the IBD infusion unit, enabling a pre-admission order of IV therapy. This system sends an automated email to the patient the day before the admission. Using the secured link in this email, the patient is required to answer several red flag and open questions about their health status since the previous infusion. These answers are reviewed by the healthcare provider and, if approved, the IV therapy is ordered and prepared for subsequent administration at arrival on the infusion unit. All patients treated with IV therapy at the IBD clinic of our hospital were invited to participate in this program, which was GDPR (General Data Protection Regulation) approved. Time consumption was prospectively evaluated in patients with maintenance infliximab treatment (one hour infusion) before and after implementation in June 2018.

Results : In total 172 IBD patients ($n=77$ male, $n=119/51$ Crohn/ulcerative colitis, $n=112/60$ infliximab/vedolizumab) were invited to the program, 150 (87%) of which accepted to participate and 22 (13%) declined. The most important reason to decline participation was the lack of email access, which can be attributed to the median age of this subgroup (median age 73y (IQR 65-75) vs. 46y (IQR 36-56); $p<0.0001$). Inclusion rates were not influenced by gender, disease type or treatment duration. The effective adoption of the e-health system (number of IV therapies ordered online) increased from 42% in the first month to 59% in the fifth month. The use of the e-health system reduced the median admission time at the infusion unit significantly from 169 min (IQR 153-192) to 108 min (IQR 101-122) ($p<0.0001$) in infliximab-treated patients.

Conclusions : The use of an e-health pre-admission assessment and order system for IV therapy in IBD is feasible, well adopted and leads to a significant reduction in admission time.

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POSTOPERATIVE ENDOSCOPIC AND CLINICAL RECURRENCE AFTER ILEOCOLONIC RESECTION IN PATIENTS WITH CROHN'S DISEASE CANNOT BE PREVENTED WITH HIGH DOSE VITAMIN D. J. de Bruyn (1), P. Bossuyt (2), M. Ferrante (3), R. West (4), G. Dijkstra (5), B. Witteman (6), D. Franchimont (7), J. van der Bilt (8), T. Tollens (9), W. Bemelman (10), A. D'hoore (11), M. Duijvestein (12), G. D'haens (1) / [1] Amsterdam UMC, Amsterdam, The Netherlands, Department of Gastroenterology and Hepatology, [2] Imeldaziekenhuis, Bonheiden, Belgium, Department of Gastroenterology and Hepatology, [3] University Hospitals Leuven, Belgium, Department of Gastroenterology and Hepatology, [4] Franciscus Gasthuis & Vlietland, The Netherlands, Department of Gastroenterology and Hepatology, [5] University Medical Center Groningen, The Netherlands, Department of Gastroenterology and Hepatology, [6] Gelderse Vallei Hospital, The Netherlands, Department of Gastroenterology and Hepatology, [7] Erasmus

Hospital, Brussels, Belgium, Department of Gastroenterology and Hepatology, [8] Flevoziekenhuis, The Netherlands, Department of Surgery, [9] Imelda Hospital, Bonheiden, Belgium, Department of General and Abdominal Surgery, [10] Amsterdam UMC, Amsterdam, The Netherlands, Department of Surgery, [11] University Hospitals Leuven, Belgium, Department of Abdominal Surgery, [12] Amsterdam UMC, Amsterdam, The Netherlands, Gastroenterology and Hepatology.

Introduction : Vitamin D deficiency is common amongst patients with Crohn's disease (CD). Previous preclinical experiments and one clinical trial suggested anti-inflammatory effects of vitamin D in IBD.

Aim : We performed a prospective placebo controlled clinical trial in patients with CD undergoing an ileocolonic resection with ileocolonic anastomosis in which we studied the potential anti-inflammatory effects of vitamin D.

Methods : This trial was performed in 17 centres in Belgium and the Netherlands. CD patients with at least 1 risk factor for recurrence were randomized to receive weekly 25.000 International Units (IU) of vitamin D3 (Cholecalciferol in 1 milliliter vials, SMB Pharma, Brussels, Belgium) or placebo for 6 months following their first or second ileocolonic resection. All other CD medication was stopped. The primary endpoint at week 26 was endoscopic recurrence defined as a modified Rutgeerts score ≥ 2 (>5 aphthous ulcerations in the neoterminal ileum, with or without anastomotic lesions); secondary endpoints included clinical recurrence (Crohn's disease activity index (CDAI) ≥ 220), quality of life (SF-36, IBD-Q and EQ-5D), safety and differential outcomes by baseline vitamin D serum concentrations. All endoscopies were centrally read and adjudicated by two expert blinded endoscopists. ClinicalTrials.gov ID NCT02010762, funding by IOIBD and BROAD

Results : 143 patients were randomized (72 to vitamin D and 71 to placebo); baseline patient characteristics were comparable between the two groups (mean age (\pm SD) 34 (\pm 12) vs 37 (\pm 15) years, and 38% vs 40% male, respectively). Serum 25-OH vitamin D levels increased from median (IQR) 42 (27–56) nmol/L to 87 (73–105) nmol/L at week 26 in the intervention group ($p < 0.00001$), and remained unchanged at 43 (29–64) nmol/L in patients on placebo throughout the whole study. No difference was seen in the incidence and severity of endoscopic recurrence at 26 weeks between the two groups (Table 1). In addition, the cumulative clinical recurrence rates at week 26 were also comparable (Table 1). Quality of life as measured by SF-36, IBD-Q and EQ-5D improved slightly over time in both groups but was not significantly different between the two groups. Adverse events were uncommon in either group; adverse events with an incidence $>5\%$ included abscess formation in both groups and wound infection in the placebo group, and were related to surgery. Outcome was not affected by baseline serum vitamin D level, season of inclusion, or ethnicity.

Conclusions : High-dose vitamin D treatment did not reduce the incidence of postoperative endoscopic and clinical recurrence in CD patients, despite normalization of serum 25-OH vitamin D concentrations. Hence, vitamin D deficiency might merely be a consequence of disease activity rather than a causal explanation in the pathophysiology of CD.

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IMMUNOGENICITY IS NOT THE DRIVING FORCE OF TREATMENT FAILURE IN VEDOLIZUMAB-TREATED INFLAMMATORY BOWEL DISEASE PATIENTS. N. Van Den Berghe (1), B. Verstockt (2), S. Tops (1), M. Ferrante (2), S. Vermeire (2), A. Gils (1) / [1] Laboratory for Therapeutic and Diagnostic Antibodies, KU Leuven, Leuven, Belgium, Department of Pharmaceutical and Pharmacological Sciences, [2] University Hospitals Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction : The pivotal GEMINI trials reported low immunogenicity (4%) of vedolizumab during treatment. However, 16 weeks after treatment discontinuation, 10% of patients were anti-vedolizumab antibody (AVA) positive using a drug-sensitive assay. AVA are frequently underestimated since most assays are not drug-tolerant and unable to detect anti-drug antibodies while there is drug in the circulation.

Aim : This study aimed to explore which anti-drug antibody assay is best suited to detect AVA and investigated immunogenicity of vedolizumab in inflammatory bowel disease (IBD) patients discontinuing vedolizumab therapy.

Methods : A drug-tolerant assay was developed for the measurement of AVA in the presence of vedolizumab and compared to the previously established drug-sensitive (lower limit of quantification (LLOQ) = 5 ng/ml) and drug-resistant (LLOQ = 3800 ng/ml) assay by application on samples of IBD patients with proven AVA levels (Bian et al., IBD 2017). After selection of the most suitable assay, vedolizumab and AVA were measured at week 6, at the last infusion and 12-20 weeks after treatment discontinuation in a cohort of 40 vedolizumab-treated IBD patients who stopped treatment due to primary non-response ($n = 23$), loss of response ($n = 8$), adverse events ($n = 7$) or a combination ($n = 2$).

Results : The drug-tolerant assay had a LLOQ of 350 ng/ml and could detect AVA in 20 samples compared to 1 and 10 samples with the drug-sensitive and drug-resistant assay, respectively. Using the drug-tolerant assay, three (8%) out of 40 vedolizumab-treated IBD patients who discontinued therapy were AVA positive at week 6. All three patients also had AVA at least at one other time point. These three patients, as well as the other 37 did not have AVA at the time of the last infusion nor after treatment discontinuation. The median week 6 vedolizumab concentration of 40 patients who discontinued therapy was 23.2 μ g/ml (IQR 14.7-31.9 μ g/ml). Primary non-responders had numerically lower median

vedolizumab concentrations at week 6 compared to patients with loss of response (20.3 vs 30.7 µg/ml, respectively, $p = 0.0570$). Vedolizumab week 6 concentrations of patients who stopped therapy due to adverse events were comparable to those of patients with loss of response.

Conclusions : Immunogenicity of vedolizumab is not the driving force of treatment failure and AVA do not increase upon treatment discontinuation in vedolizumab-treated IBD patients. We hypothesize that clinicians can stop and restart vedolizumab without the risk of adverse events or a diminished clinical response due to anti-drug antibodies. Additionally, our data suggests that underexposure during induction might partially be responsible for primary non-response.

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ULTRA-PROACTIVE THERAPEUTIC DRUG MONITORING INCORPORATING INFLIXIMAB POINT-OF-CARE TESTING WITH AD HOC DOSE ADJUSTMENT REDUCES C-REACTIVE PROTEIN LEVELS IN PATIENTS WITH IBD DURING INFLIXIMAB MAINTENANCE TREATMENT. P. Bossuyt (1), E. Hoefkens (1), I. Geerts (2), F. Verbiest (3), E. Vermeulen (2), A. Van Olmen (1), L. Pouillon (1) / [1] Imelda Hospital, Bonheiden, Belgium, Department of gastroenterology, [2] Imelda Hospital, Bonheiden, Belgium, Department of laboratory medicine, [3] Imelda Hospital, Bonheiden, Belgium, Hospital Pharmacy.

Introduction : Therapeutic drug monitoring (TDM) of infliximab (IFX) improves patient outcomes and is cost-effective. The short turnaround time of point-of-care testing (POCT) allows ad hoc dose adjustment.

Aim : We aimed to determine the feasibility and pilot effectiveness of an ultra-proactive TDM algorithm including POCT of IFX in patients with inflammatory bowel disease (IBD).

Methods : All IBD patients with maintenance IFX treatment at our referral IBD clinic were prospectively included between June and August 2018. An ultra-proactive IFX TDM algorithm was applied as follows. All patients had an ELISA trough level (TL) measurement at baseline, of which the result determined the follow-up pathway: (A) TL between 3-7µg/mL: continuation at same dose and interval; (B) TL >7µg/mL: interval prolongation allowed; (C) TL <3µg/mL: interval shortening with minimum 2 weeks, with the next IFX TL measured using a POCT. (i) If the POCT showed an IFX TL <3µg/mL, dose was optimized ad hoc using a linear dosing formula ($\text{Dose } n = (\text{TL target} * \text{Dose } n-1) / \text{TL measured}$), followed by a new POCT test at next visit with the same interval. (ii) If the POCT showed an IFX TL $\geq 3\mu\text{g/mL}$, no additional dose was given and routine TL testing with ELISA was retaken at next visit. Physician's global assessment, C-reactive protein (CRP), haemoglobin and albumin levels were sequentially evaluated according to standard of care.

Results : In total, 115 patients were included (Crohn's disease/ulcerative colitis/IBDU $n=80/34/1$; median CRP 1.2 mg/L (IQR 0.6-3.8); median TL 4.6 µg/mL (IQR 2.6-7.4)). A median of 3 infusions (IQR 3-4) during follow-up led to a total number of 371 TL measurements. There was a significant drop of low TL (<3µg/mL) over time (38/115 at baseline vs 22/256 during follow-up; $p=0.0001$). The need for POCT reduced from an initial 28% to 8.7% ($p=0.0001$). Additional dosing based on POCT measurement was needed in 7/43 (16.3%) cases. Patients needing ad hoc dose adjustment after interval shortening had significant lower TL at the previous measurement than those who did not (median (IQR) TL 0.9 µg/mL (0.7-1.8) vs. 2.3 µg/mL (1.5-2.6); $p=0.036$). An IFX TL cut off of 1 µg/ml predicted an ad hoc extra dose after interval shortening with a NPV of 96% (90% sens, 75% spec). In patients with elevated CRP at baseline ($n=26$), ultra-proactive TDM resulted in a significant reduction of CRP over time, with a median (IQR) of 7.8 (6.5-18.3) mg/L at baseline compared with 6.3 (4-9.9) mg/L during follow-up ($p=0.025$).

Conclusions : Ultra-proactive TDM based on a strict algorithm including POCT and ad hoc dose adjustment is feasible and significantly lowers CRP levels in IBD patients treated with maintenance IFX. Less than 10% of patients need POCT over time.

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PHARMACOKINETIC AND PHARMACODYNAMIC EVALUATION OF RADIOLOGICAL HEALING IN CROHN'S DISEASE PATIENTS TREATED WITH INFLIXIMAB: A TAILORIX MRE SUBSTUDY. P. Bossuyt (1), E. Dreesen (2), J. Rimola (3), S. Devuysere (4), Y. De Bruecker (4), R. Vanslebrouck (5), L. Valérie (6), M. Zappa (7), C. Savoye-Collet (8), A. Gils (2), S. Vermeire (9), L. Peyrin-Biroulet (10) / [1] Imelda Hospital, Bonheiden, Belgium, Department of gastroenterology, [2] Catholic University of Leuven, Leuven, Belgium, Department of Pharmaceutical and Pharmacological Sciences, [3] Hospital Clinic of Barcelona, Barcelona, Spain, IBD unit, Radiology Department, [4] Imelda Hospital, Bonheiden, Belgium, Department of radiology, [5] University Hospital, Gasthuisberg, Leuven, Belgium, , Belgium, Department of radiology, [6] Nancy University Hospital, Vandoeuvre-lès-Nancy, France, INSERM U947 and Department of Radiology, [7] Beaujon Hospital, Clichy, France, Department of radiology, [8] Rouen University Hospital, Rouen University Hospital, Rouen, France, Department of radiology, [9] University Hospital Gasthuisberg, Leuven, Belgium, Department of gastroenterology and hepatology, [10] Nancy University Hospital, Vandoeuvre-lès-Nancy, France, INSERM U954 and Department of Hepato-Gastroenterology.

Introduction : Higher infliximab (IFX) trough levels (TL) are associated with clinical and endoscopic remission in Crohn's disease (CD). The relationship between pharmacokinetic (PK) and pharmacodynamic (PD) monitoring and radiological healing evaluated by magnetic resonance enterography (MRE) are unknown.

Aim : We here assessed the correlation between IFX TL and radiologic remission in a post hoc analysis of the prospective randomized TAILORIX trial (1).

Methods : This study included all patients from TAILORIX that had baseline and week (w) 54 MRE available. The MARIA score was calculated by two independent blinded central readers (CR). In case of discrepancy a third CR provided adjudication. Radiologic response and remission were defined as MARIA in all segments <11 and <7 respectively. Prospectively collected PK markers (IFX TL), PD markers (CRP and Faecal Calprotectin [FC]) and endoscopic remission (CD endoscopic index of severity, CDEIS <3) were used for the analysis.

Results : Thirty-six patients were included in the analysis (50% female; median age 35.7y IQR 25.6-48.6; median disease duration 1.44 months IQR 0.6-22.4). Radiologic response and remission at w54 was 32.3% and 25.8% respectively; endoscopic remission was 67.7%. The correlation between CDEIS and MARIA at w0 was moderate (Pearson 0.46; $p=0.008$), but was absent at w54. No correlation could be found between endoscopic and radiologic remission. Radiological remission at w54 was correlated with IFX TL at week 14 ($p=0.049$) with a ROC based IFX TL cut off value of 7.8 $\mu\text{g/ml}$ (AUC 0.74 sens 75% and spec 86%; NPV 90% and PPV 67%). Radiologic response at w54 was correlated with IFX TL at w14 ($p=0.048$) with a ROC based IFX TL cut off value of 7.8 $\mu\text{g/ml}$ (AUC 0.73 sens 75% and spec 90%; NPV 87% and PPV 78%) and with continuous pharmacological response (IFX TL >5.0 $\mu\text{g/ml}$ at all time points) ($p=0.034$). No difference was found in IFX TL comparing patients with or without radiologic remission or response at W54. A subgroup of 21 patients needed dose escalation. In this subgroup continuous pharmacological response (IFX >7 $\mu\text{g/ml}$ at all time points) was associated with radiological response ($p=0.042$) and remission ($p=0.010$). CRP and FC were not associated with radiological remission or response at any given time point.

Conclusions : In this post hoc analysis of TAILORIX, radiologic response and remission following infliximab induction and maintenance were observed in 32 and 26% of patients. IFX TL >7.8 $\mu\text{g/ml}$ at the end of induction therapy predicted both radiologic remission and response at w54 in patients with CD. Reference: 1. D'Haens G et al. *Gastroenterology* 2018; 154(5): 1343-51.e1.

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PNEUMOCYSTIS JIROVECI PNEUMONIA IN IBD PATIENTS TREATED WITH IMMUNOMODULATOR(S). S. Vieujean (1), A. Moens (2), K. Rothfuss (3), E. Savarino (4), S. Vavricka (5), C. Reenaers (1), M. Ferrante (2), J. Rahier (6), E. Ecco Confer Investigators. (7) / [1] University Hospital of Liège, Liège, Belgium, Department of Gastroenterology, [2] University Hospitals Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology, [3] Robert-Bosch-Hospital, Stuttgart, Germany, Department of Gastroenterology and Hepatology, [4] University of Padua, Padua, Italy, Department of Gastroenterology, [5] University Hospital, Zurich, Switzerland, Department of Gastroenterology and Hepatology, [6] CHU UCL Namur, Yvoir, Belgium, Department of Gastroenterology and Hepatology, [7] ECCO CONFER investigators, Vienna, Austria, ECCO CONFER investigators.

Introduction : Pneumocystis jirovecii Pneumonia (PJP) is a very rare life-threatening pulmonary fungal infection that occurs in immunocompromised individuals including patients with inflammatory bowel disease (IBD). Prophylaxis for PJP is recommended in IBD patients treated with triple immunomodulators where one agent is a calcineurin inhibitor or an anti-TNF α (Rahier et al. 2014) but there is no consistency in a preventive approach in patients with double or single immunomodulators.

Aim : Our aim was to describe the immunosuppressive treatment profile of IBD patients infected with PJP as well as the outcome of the disease.

Methods : Cases of PJP were retrospectively collected through the COLlaborative Network For Exceptionally Rare case reports of the European Crohn's and Colitis Organization (ECCO CONFER). All ECCO members were invited to report cases of PJP. Data were collected through a case report form.

Results : A total of 15 PJP infections were reported in 14 IBD patients (9 ulcerative colitis and 5 Crohn's disease including 10 men and 4 women). The median age at PJP diagnosis was 55 years (IQR 44-80). Diagnosis was performed by a positive PJ polymerase chain reaction on the bronchoalveolar lavage in 87% of the cases and by a microscopic direct exam in 7% (unreported in 1 patient). One patient was coinfecting by HIV and 57% were non-smokers. Immunosuppressive therapies at the time of diagnosis included steroids (n=11), thiopurines (n=9), infliximab (n=3), cyclosporin (n=2), methotrexate (n=1) and tacrolimus (n=1). Two PJP occurred in patients on triple immunosuppression (steroid, thiopurine and cyclosporin). Nine patients had a double immunosuppression (steroid and thiopurine (n=4), infliximab and thiopurine (n=2), steroid and infliximab (n=1), steroid and methotrexate (n=1) and steroid and tacrolimus (n=1)). Three patients were on monotherapy (steroid (n= 2) and thiopurine (n=1)). PJP in the HIV patient occurred in absence of immunosuppressive treatment. None of the patients diagnosed with PJP had received prophylaxis. All patients were treated by trimethoprim/sulfamethoxazole or atovaquone and 5 required an intensive care unit stay. Two

patients (14%) died and 1 patient had a recurrent episode 16 months after initial treatment. Evolution was favourable for the others

Conclusions : This case series reports PJP in IBD patients while on single or double immunosuppression highlighting the risk in this population. Identifying risk factors for PJP infection in the IBD patients is essential to provide a case-by-case prophylaxis.

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EFFICACY AND SAFETY OF BIOLOGICAL THERAPIES IN CHRONIC ANTIBIOTIC-REFRACTORY POUCHITIS: A RETROSPECTIVE SINGLE CENTRE EXPERIENCE. B. Verstockt (1), C. Claeys (1), G. Van Assche (1), A. D'hoore (2), A. Wolthuis (2), S. Vermeire (1), M. Ferrante (1) / [1] University Hospitals Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] University Hospitals Leuven, Leuven, Belgium, Department of Abdominal Surgery.

Introduction : Chronic antibiotic-refractory pouchitis affects up to 15% of patients with ulcerative colitis (UC) following colectomy with ileal pouch-anal anastomosis (IPAA). In retrospective series, infliximab (IFX), adalimumab (ADM) and vedolizumab (VDZ) have demonstrated efficacy, but data are limited.

Aim : We here report single centre data of biological therapy in refractory pouchitis.

Methods : We retrospectively assessed all records from UC patients who underwent IPAA and were exposed to IFX, ADM or VDZ thereafter at our centre. Patients with a baseline modified pouchitis disease activity index (mPDAI) < 5 or with Crohn's disease related complications of the pouch were excluded. Clinically relevant remission, defined as a mPDAI < 5 and a reduction of mPDAI 2 points from baseline, was assessed at week 14. Non-responder imputation was applied in case of discontinuation prior to week 14.

Results : Thirty-three unique patients were included (69.7% male, median [IQR] age 39.6 [33.7-52.8]). Three (9.1%) underwent colectomy because of high grade dysplasia, whereas 90.9% had surgery due to refractory UC. Prior to surgery, patients had been exposed to cyclosporine (n=14), IFX (n=12), ADM (n=3), and/or VDZ (n=3). J-pouches were constructed mainly in (modified) 2-stage (n=25) procedures. All developed chronic antibiotic-refractory pouchitis after a median of 3.1 years, for which they received IFX (n=23), ADM (n=13) or VDZ (n=15). Clinically relevant remission at week 14 was observed in 43.5% of IFX group, and 38.5% and 60.0% in the ADM and VDZ group. With a median follow-up of 1.0 (0.3-3.1) years, significantly more patients continued VDZ compared to anti-TNF therapy (HR 2.9 [95% CI 1.1-8.5], p=0.04). Compared to baseline, VDZ resulted in a significant drop in endoscopic PDAI score at final follow-up (p=0.004), whereas IFX and ADM led to a more modest drop (p=0.03, p=0.1 respectively). Adverse events (mainly infusion reactions) and undetectable serum levels explained 48.1% of the patients discontinuing anti-TNF therapy, whereas discontinuation of VDZ was only related to insufficient efficacy. Overall, 4 patients (12.1%) ended up with a permanent ileostomy.

Conclusions : In this case series, the use of anti-TNF agents for the treatment of chronic antibiotic-refractory pouchitis was hampered by the high rate of adverse events partly related by pre-colectomy exposure to the same drug. Therefore, VDZ might be an efficacious and safe alternative, which is currently being studied in a phase IV randomized placebo-controlled trial.

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SEROLOGICAL MARKERS ASSOCIATED WITH DEVELOPMENT OF POUCHITIS AFTER ILEAL POUCH-ANAL ANASTOMOSIS. K. Machiels (1), M. Ferrante (2), N. Davani Ardeshir (2), A. Wolthuis (3), A. D'hoore (3), S. Vermeire (2) / [1] University Hospitals Leuven, Leuven, Belgium, Translational Research Center for Gastrointestinal Disorders (TARGID), [2] University Hospitals Leuven, Belgium, Translational Research Center for Gastrointestinal Disorders (TARGID), [3] University Hospitals Leuven, Belgium, Department of abdominal surgery.

Introduction : Pouchitis is the most common complication in patients with ulcerative colitis (UC) requiring ileal pouch anal anastomosis (IPAA). Pouchoscopy remains the gold standard to diagnose pouchitis in the absence of other surrogate biomarkers.

Aim : We performed serum proteomic profiling to identify biomarkers that could be predictive and discriminative for the development of pouchitis following IPAA.

Methods : This was a prospective cohort study in 51 patients undergoing IPAA at our center (46 UC and 5 familial adenomatous polyposis patients). Serum was collected before colectomy and at predefined clinical visits at month 1, 3, 6 and 12 after IPAA. At every clinical visit, patients had endoscopic evaluation of the pouch. Pouchitis was defined by presence of endoscopic inflammation. Serum samples from 62 age- and sex matched healthy subjects (HS) served as controls. A panel of 91 inflammation-related proteins was measured using Proximity Extension Assay (Olink). Analyses

were performed in SPSS and R. False discovery rate (FDR)-corrected p-values were reported as FDR. Logistic regression and receiver operating characteristic curve analysis were used to evaluate the predictive and discriminative power of significant biomarkers and clinical variables (cutoff $p < 0.1$). Pathway analyses was conducted using STRING database.

Results : A total of 17 (37%) UC patients were diagnosed with pouchitis during the first year after IPAA. Younger age at colectomy (OR=1.11, 95%CI=1.03-1.21; $p=0.008$) and backwash ileitis (OR=8.37, 95%CI=1.06-65.9; $p=0.04$) were associated with pouchitis. When comparing the protein profiles prior to colectomy in UC patients developing pouchitis (UC-P) and UC patients with normal pouches (UC-NP), we observed respectively 42 and 45 proteins significant from the profiles in HS (FDR<0.05). The majority ($n=35$) were overlapping between UC-P and UC-NP. Ten proteins (\uparrow OPG, MCP1, CCL4, MCP4, MMP1, CD5, 4EBP1, EN-RAGE; \downarrow FIt3L, CCL25) were uniquely different in UC-P (FDR<0.05) and pathway analyses indicated an involvement of these proteins in the regulation of NK cell chemotaxis and cellular extravasation. No pathways were detected for the 7 uniquely dysregulated proteins (\uparrow TSLP; \downarrow CD244, uPA, SCF, FGF5, IL12B, NT3) in the UC-NP comparison. Similarly, comparison of baseline protein profiles of UC-NP and UC-P with FAP, revealed respectively 7 and 17 significant proteins ($p < 0.05$), of which 14 solely dysregulated in the UC-P comparison. Combination of HGF, TNFRSF9 and age at colectomy was the most accurate to predict development of pouchitis within 1 year (AUC=0.875). A panel of 4 proteins (IL17A, CXCL1, CCL25 and TRAIL) showed a good discriminative power (AUC=0.984) to diagnose pouchitis at month 12 post-IPAA. The impact of colectomy with IPAA on the serological proteins was different in UC-NP and UC-P. UC-NP showed a significant decrease of OSM, TGF α , IL24 and FGF19 (FDR<0.05), which are involved in MAPK and JAK-STAT cascades, whereas CDCP1, uPA, TRANCE, IL12N, CCL25, TNFRSF9 and TNFB, of which multiple proteins are involved in response to wounding and tissue remodeling, increased post-IPAA (FDR<0.05). In contrast, no significant temporal changes were detected in UC-P.

Conclusions : Before colectomy, there is a great overlap in serum protein profiles between patients who do or do not develop pouchitis. We found that proteins involved in NK cell chemotaxis and cellular extravasation were dysregulated solely in patients developing pouchitis. HGF and TNFRSF9 in combination with age at colectomy were predictive for pouchitis and we identified a combination of 4 biomarkers with diagnostic potential. Further validation in a larger cohort is required.

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EFFECTIVENESS AND SAFETY OF VEDOLIZUMAB MAINTENANCE THERAPY FOR INFLAMMATORY BOWEL DISEASE: FINDINGS FROM A BELGIAN REGISTRY. E. Louis (1), V. Muls (2), P. Bossuyt (3), A. Colard (4), A. Nakad (5), D. Baert (6), F. Mana (7), P. Caenepeel (8), S. Vanden Branden (9), S. Vermeire (10), F. D'heygere (11), B. Strubbe (12), A. Cremer (13), J. Coche (14), V. Setakhr (15), F. Baert (16), A. Vijverman (17), J. Coenegrachts (18), F. Flamme (19), A. Hantson (20), K. Wijnen (20), E. Piters (20), G. Hantsbarger (21), F. Wan (21), B. Jiang (21), P. Dolin (22) / [1] University Hospital CHU of Liège, Liege, Belgium, Department of gastroenterology, [2] Saint-Pierre University Hospital, Brussels, Belgium, Department of Gastroenterology, [3] Imeldaziekenhuis, Bonheiden, Belgium, Department of Gastroenterology, [4] Hopital CHC Liège, Belgium, Department of gastroenterology, [5] CHwapi Notre Dame, Tournai, Belgium, Department of gastroenterology, [6] Maria Middelaes Medical Centre, Ghent, Belgium, Department of Gastroenterology, [7] UZ Brussel, Vrije Universiteit Brussel, Brussels, Belgium, Department of Gastroenterology, [8] Ziekenhuis Oost Limburg, Genk, Belgium, Department of Gastroenterology, [9] OnzeLieveVrouwziekenhuis, Aalst, Belgium, Department of Gastroenterology, [10] University Hospitals Leuven, Leuven, Belgium, Department of Gastroenterology, [11] AZ Groeninge Hospital, Kortrijk, Belgium, Department of Gastroenterology, [12] AZ St Lucas, Ghent, Belgium, Department of Gastroenterology, [13] Hopital Universitaire Erasme, Brussels, Belgium, Department of Gastroenterology, [14] Clinique Saint-Pierre, Ottignies, Belgium, Department of gastroenterology, [15] CHU UCL Namur site Sainte Elisabeth, Brussels, Belgium, Department of gastroenterology, [16] AZ Delta, Roeselare, Belgium, Department of gastroenterology, [17] Hospital CHR de la Citadelle, Liège, Belgium, Department of gastroenterology, [18] Jessa Ziekenhuis, Hasselt, Belgium, Department of gastroenterology, [19] CHU Ambroise Paré, Mons, Belgium, Department of gastroenterology, [20] Takeda Pharmaceuticals Belgium, Brussels, Belgium, Medical Affairs, [21] Takeda Pharmaceuticals Company, USA, Boston, United States (the), Statistics, [22] Takeda Pharmaceuticals UK, London, United Kingdom (the), Epidemiology.

Introduction : Clinical trials have demonstrated the efficacy and safety of vedolizumab (VDZ) as maintenance therapy for Crohn's disease (CD) and ulcerative colitis (UC). This report presents outcome data for VDZ maintenance therapy in real life practice in Belgium.

Aim : The aim of this study was to evaluate the safety and efficacy of vedolizumab maintenance therapy in the Belgian real life setting.

Methods : The Belgium VDZ Registry includes 202 VDZ treated adult patients from 19 Belgian centres. Inclusion criteria were ongoing VDZ therapy started 15+ days prior to recruitment and patient not in a clinical trial or VDZ PASS study. This interim analysis presents safety data for the all 202 registry participants, and clinical remission rates on the subset of 156 participants with at least one 6 monthly investigator update on clinical management and outcomes. Clinical remission was defined as HarveyBradshaw Index < 5 or partial Mayo Score < 3 with no subscore > 1 . Patients who

discontinued VDZ were considered not in remission from that point forwards. An imputation analysis was included to account for missing disease activity scores, where a missing activity score was assumed not in remission, thereby giving a minimum imputation estimate.

Results : The characteristics of the 202 participants were 52% female, 66% had CD, predominantly ileal or ileocolonic CD, and 34% had UC, predominantly left-sided UC. Median age at onset of IBD was 28 years, and median duration of IBD prior to starting VDZ was 10 years. At recruitment, median length of ongoing VDZ therapy was 11 months, and 63% of UC and 60% of CD patients were in remission. Median duration of follow-up in the outcomes subset was 11 months (range 4-18 months). Clinical remission rates for CD patients as per duration of maintenance VDZ therapy were: 1-6 months: As observed: 64% - Imputation: 47% 7-12 months: As observed: 48% - Imputation: 36% 13-24 months: As observed: 40% - Imputation: 34% 25-36 months: As observed: 30% - Imputation: 23% For UC patients, the clinical remission rates as per duration of maintenance VDZ therapy were: 1-6 months: As observed: 54% - Imputation: 33% 7-12 months: As observed: 80% - Imputation: 51% 13-24 months: As observed: 70% - Imputation: 55% 25-36 months: As observed: 52% - Imputation: 42% The corresponding rates of corticosteroid-free clinical remission were 30-40% for both CD and UC. All reported serious adverse events (SAEs) and nonserious AEs were considered unrelated to VDZ therapy. 34 patients (16.8%) had a SAE, the most frequent being worsening of CD/UC (4.0%) and small intestine obstruction (1.5%). 80 patients (39.6%) had a nonserious AE, the most frequent being constipation (2.5%), gastroenteritis (2.0%), nasopharyngitis (2.0%), and upper respiratory tract infection (2%). There were no reports of hepatic injury, infusion-related reactions, hypersensitivity or opportunistic infection.

Conclusions : These real-life data collected from 19 gastroenterology centres across Belgium demonstrate sustained clinical benefit with up to 36 months of VDZ maintenance therapy in everyday clinical practice.

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THE IMPACT OF STORAGE TIME AND FREEZE-THAW CYCLES ON FAECAL CALPROTECTIN CONCENTRATION IN INFLAMMATORY BOWEL DISEASE PATIENTS AND CONTROLS. C. Caenepeel (1), K. Machiels (2), S. Vieira-Silva (3), M. Ferrante (2), S. Vermeire (2) / [1] KU Leuven, Leuven, Belgium, Departement Chronische Ziekten, Metabolisme en Veroudering, [2] KU Leuven, Belgium, Departement Chronische Ziekten, Metabolisme en Veroudering, [3] Rega Institute for Medical Research, Leuven, Belgium, Microbiology and Immunology.

Introduction : Faecal calprotectin (FCal) is considered the best surrogate marker of mucosal inflammation and therefore routinely used for diagnosis and follow-up of inflammatory bowel disease (IBD). For practical reasons, freezing the faecal sample prior to FCal extraction would be beneficial. However, freeze-thawing might degrade neutrophils, potentially leading to false positive FCal measurement. We investigated the effect of multiple freeze-thaw cycles as well as long-term storage on FCal stability in frozen faecal samples and faecal extracts.

Aim : We investigated the effect of multiple freeze-thaw cycles as well as long-term storage on FCal stability in frozen faecal samples and faecal extracts.

Methods : Fresh faecal samples from ten healthy controls (HC) and ten active IBD patients were collected in March 2017 and split into five tubes. Each tube was stored differently until extraction: (I) 4°C for 1 day, (II-IV) immediately frozen at -80°C for 1 week and next subjected to 1, 2 and 3 freeze-thaw cycles, and (V) immediately frozen at -80°C for 1.5 years. During a freeze-thaw cycle, the tubes of all samples were thawed for 1h, a FCal extract was prepared from one tube. The remaining tubes were stored at -80°C. The Bühlmann® Smart Prep Faecal Sample Preparation Kit and Bühlmann® FCalTM ELISA kit were used for respectively FCal extraction and measurement. From condition I-IV, an additional aliquot of the calprotectin extract was stored at -20°C for 1.5 years (VI). Statistical analyses were performed in JMP. Linear regression analysis was performed to compare the FCal concentrations. Root mean square errors (RMSE) demonstrate the average difference between the FCal measurements.

Results : The median FCal concentration in respectively the HC and IBD group were 30 and 852 µg/g faeces. The RMSE comparing the first FCal concentration (fresh) with respectively the 2nd, 3th and 4th FCal concentration was 11.5, 18 and 27 µg/g faeces in the HC group and 327, 71 and 274 µg/g faeces in the IBD group. Freeze-thawing (II-IV) resulted in both ascending and descending deviations from the fresh FCal concentrations. Long-term storage (V) vs fresh (I) indicated a RMSE of 20 µg/g faeces in the HC group and 179 µg/g faeces in the IBD group. Long-term storage of the FCal extract vs fresh resulted in a RMSE of respectively 9 and 105 µg/g faeces in the HC group and IBD group. In HC, FCal concentrations did not exceed 100 µg/g faeces, neither after different freeze-thaw cycles nor after long-term storage, except for one sample that went up to 123 µg/g faeces after three freeze-thaw cycles. One IBD patient switched from a commonly regarded positive calprotectin to a negative calprotectin (254 vs. 154 µg/g faeces) after 1.5 years storage

Conclusions : Multiple freeze-thaw cycles and long-term storage of faecal samples and FCal extracts influence FCal concentrations only moderately, and without influence on clinical decision-making. The non-consistent variation between different conditions is more likely caused by existing within-stool variability and variation in technical execution, rather than by freeze-thawing or storage duration. For further clinical use and research, freezing and long-term storage are acceptable to perform reliable FCal measurements.

FAECAL MICROBIOTA TRANSPLANTATION AS TREATMENT FOR RECURRENT CLOSTRIDIUM DIFFICILE INFECTIONS: A SINGLE CENTRE EXPERIENCE. C. Caenepeel (1), A. Schroë (2), M. Ferrante (2), S. Vermeire (2) / [1] KU Leuven, Leuven, Belgium, Departement Chronische Ziekten, Metabolisme en Veroudering, [2] KU Leuven, Belgium, Departement Chronische Ziekten, Metabolisme en Veroudering.

Introduction : Clostridium difficile infection (CDI) is a significant complicating factor in inflammatory bowel disease (IBD). IBD patients with CDI appear to flare worse than their non-IBD counterparts. Fecal microbiota transplantation (FMT) is recently recommended to effectively treat recurrent CDI (rCDI). Despite, FMT is still not a routine procedure in most centers.

Aim : We describe our experience of FMT to treat rCDI in IBD patients and other indications, with focus on the identification of risk factors for FMT failure.

Methods : Patients were included retrospectively (2012-2018) if (I) CDI was confirmed in the fecal sample according to the ESCMID algorithm and (II) patients failed ≥ 2 antibiotics for CDI or had ≥ 2 laboratory-confirmed CDI recurrences. Demographic and clinical data were collected (age, sex, body mass index, underlying gastro-intestinal problems, IBD, medication use, predisposing infection, hospital acquired infection, amount of antibiotic treatments before FMT, days between first positive faecal sample and first FMT, relationship with donor, severity of CDI and failure of previous vancomycin treatment). FMT success was defined as resolution of diarrhoea within 48h, for ≥ 8 weeks. Statistical analyses were performed in JMP.

Results : We included 33 rCDI patients in which 8 IBD patients, 8 post-lung or kidney transplant patients and 1 patient with multiple-sclerosis. 15 of these 33 patients were on immunosuppressive therapy during their first FMT. FMT success was seen in 24/33 patients (72.7%) after 1 FMT. This success ratio was not significantly different in IBD patients (Fisher exact test $p=0.37$) or post-transplant patients ($p=0.94$), or for all immunocompromised patients combined ($p=0.741$). Relapses were observed in 9/33 patients (27.3%) within 8 weeks and in 3/33 patients (9.1%) later on. Nine relapsed patients underwent a second FMT which was successful in 5 patients (4 received a different donor). The remaining 3 patients were successfully treated with a vancomycin based scheme (pulse or taper). FMT was not efficacious in 7/33 patients (%). The overall cumulative success ratio was 78.8% with minimal side effects in 6 of the 44 FMT's (13.6%). None of the demographic and clinical variables was significantly correlated with success after ≥ 1 FMT's. The use of a related donor tended to show a higher effectiveness after 1 FMT ($p<0.053$). The presence of a predisposing infection treated with antibiotics gave a trend ($p<0.068$) to a lower efficacy.

Conclusions : FMT is efficacious for rCDI, also in IBD and other immunocompromised patients. Our FMT success ratios and percentage of side effects are comparable to literature. Stratification of eligible patients for FMT can be useful. However, FMT failure was not associated with any risk factor or patient group. Donor feces from a relative appears to increase FMT efficacy and multiple FMT treatment seemed to be less effective for patients with a predisposing infection.

THE PREDICTIVE ROLE OF GUT MICROBIOTA IN TREATMENT RESPONSE TO VEDOLIZUMAB AND USTEKINUMAB IN INFLAMMATORY BOWEL DISEASE. C. Caenepeel (1), S. Vieira-Silva (2), J. Vázquez-Castellanos (2), B. Verstockt (3), M. Ferrante (3), S. Vermeire (2) / [1] KU Leuven, Leuven, Belgium, Departement Chronische Ziekten, Metabolisme en Veroudering, [2] Rega Institute for Medical Research, Leuven, Belgium, Microbiology and Immunology, [3] KU Leuven, Belgium, Departement Chronische Ziekten, Metabolisme en Veroudering.

Introduction : The past decade has highlighted the central role of the gut microbiota in inflammatory bowel disease (IBD). The fecal microbiota is evolving as a useful predictive and diagnostic biomarker in the development of personalized medicine.

Aim : We here investigated if the faecal microbiota aids in predicting therapeutic response to vedolizumab (VDZ) or ustekinumab (UST) in Crohn's disease (CD) and ulcerative colitis (UC).

Methods : Faecal samples of 116 patients with IBD, treated with UST ($n=68$ CD) or VDZ ($n=30$ for CD and 18 for UC) with endoscopic active disease were collected prior to biological therapy. Quantitative microbiota phylogenetic profiling was conducted by combining 16S rRNA gene sequencing and microbial loads determination using flow cytometry. Endoscopic response in the UST cohort was defined as a 50% decrease in SES-CD score at week 24. Remission in the VDZ cohort was defined as an endoscopic Mayo-subscore of 0-1 at week 14 in UC and absence of endoscopic ulcerations endoscopy at week 24 in CD. Multivariate hyperbolic tangent neural network models (JMP) were trained to predict treatment response based on features describing the baseline fecal microbiota, clinical data (age, sex, BMI, diagnosis, disease duration and smoking) and biomarkers (C-reactive protein, albumin, hemoglobin and faecal calprotectin) or the combination. The cohorts were split in a training (2/3) and validation set (1/3). Fecal microbiota features comprised the enterotypes and quantitative abundance of taxa significantly ($P<0.1$) correlated with outcome.

Results : Ten (14.7%) UST and 27 (56.2%) VDZ patients showed endoscopic response (UST) or remission (VDZ). 13 genera correlated with treatment outcome in the VDZ cohort and 14 in the UST cohort, with 3 genera overlapping. Neural networks were trained to predict treatment response in VDZ and UST on 2/3 of the cohorts, based on baseline clinical features and biomarkers, baseline microbiota features, or both. For VDZ treatment response prediction, all models had reliable training (training: AUC=[0.71-0.87]; sensitivity=[0.62-0.88], specificity=[0.55-0.85]), but the combined model had the best validation performance (N=17; misclassification rate=31%). UST response prediction was not very reliably trained on microbiota features alone (AUC<0.70) and was also best predicted by the combined features (training AUC=0.86, sensitivity=0.88, specificity=0.33, with a validation misclassification rate of 4% (compared to 13% for the clinical and biomarkers model).

Conclusions : Our analyses do show that quantitative faecal microbiota profiling is helpful in predicting therapeutic outcome and provides valuable additional information beyond clinical features and biomarkers. Nevertheless, these predictive models were trained on still relatively small cohorts, and therefore further validation in preferably large prospective randomized cohorts is needed.

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BARIATRIC SURGERY IN INFLAMMATORY BOWEL DISEASE: OUTCOME AND SAFETY FROM A GETAID REGISTRY POPULATION. C. Reenaers (1), M. Nachury (2), C. Stefanescu (3), G. Pineton De Chambrun (4), D. Laharie (5), S. Viennot (6), J. Boileve (7), L. Peyrin-Biroulet (8), J. Grimaud (9), X. Roblin (10), F. Carbonnel (11), F. Goutorbe (12), S. Nahon (13), B. Coffin (14) / [1] CHU Sart Tilman, Liège, Belgium, hepato-gastroenterology, [2] CHRU Lille, France, Gastroenterology, [3] Hôpital Beaujon – Hôpitaux Universitaires Paris Nord Val de Seine, Clichy, France, Gastroenterology, [4] CHU Montpellier, France, Gastroenterology, [5] CHU Bordeaux, Bordeaux, France, Gastroenterology, [6] CHU CAEN, France, Gastroenterology, [7] CHU Nantes, France, Gastroenterology, [8] CHU Nancy, Nancy, France, Gastroenterology, [9] CHU Marseille, France, Gastroenterology, [10] CHU Saint-Etienne, France, Gastroenterology, [11] Hôpital universitaire Kremelin Bicêtre, Le Kremlin-Bicêtre, France, Gastroenterology, [12] Centre Hospitalier de la côte Basque, France, Gastroenterology, [13] GHI Montfermeil, France, Gastroenterology, [14] hôpital universitaire Louis-Mourier, Hôpitaux de Paris, France, Gastroenterology.

Introduction : Morbid obesity increased in the past 2 decades including in the inflammatory bowel disease (IBD) population with up to 15 to 20% of obese IBD patients in Europe and 20 to 40% in the United States. Bariatric procedures dramatically changed the management of obesity. Few data are available on the feasibility and the safety of these procedures in the IBD population.

Aim : The aim of this work was to assess the safety and the efficacy of bariatric surgery (BS) in IBD patients and to describe the outcomes of IBD after BS.

Methods : IBD patients with a history of BS were recruited in GETAID centres. The demographic and the disease characteristics were retrospectively reviewed. The type of BS, the early post-operative complications and the long-term IBD outcomes were recorded.

Results : 57 patients (44 Crohn's disease, 12 ulcerative colitis and 1 unclassified colitis) from 13 GETAID centres underwent a BS after the diagnosis of IBD. At the time of BS the mean age was 39 yrs (SD±11), the mean disease duration was 122 months (SD±77) and 42% were on biologic therapy. The BS was a sleeve gastrectomy in 44/57 (77.2%), an adjustable gastric banding in 10/57 (17.5%) and a gastric bypass in 3/57 (5.3%). Five patients (8.8%) experienced an early post-operative complication including 1 abscess with septic shock, 1 stricture of the sleeve with secondary bypass, 1 bypass converted to sleeve for peroperative technical reasons, 1 abdominal wall infection and 1 banding narrowing. The mean weight and BMI at the time of BS were 120 kg (SD±19) and 42 kg/m² (SD±5.7), respectively. The mean weight loss at maximal follow-up (median: 37.8 months - SD±35.6) post-BS was 28.3 kg (SD±15). Regarding IBD outcomes, 12 (21%) patients required a treatment modification during the follow-up period, 1 was operated for an IBD flare (ileo-caecal surgery for active Crohn's disease) and 3 experienced new perianal lesions. Anaemia was more frequent after BS (14.3% vs 5.3% pre-BS).

Conclusions : In the IBD population, BS is feasible and the sleeve gastrectomy has become the most common procedure. Close to 10% of early post-operative complications were observed in our cohort. The course of IBD was stable after the procedure with low rates of IBD complications and treatment escalations.

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COMPLIANCE TO VACCINATION GUIDELINES IN PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY DISEASES: A CROSS-SECTIONAL, SINGLE-CENTER STUDY. S. Coenen (1), D. Bertrand (2), T. Vanhoutvin (3), P. Verschueren (4), P. De Haes (3), P. De Munter (5), S. Vermeire (1), M. Ferrante (1) / [1] UZ Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology, [2] KU Leuven, Belgium, Skeletal Biology and Engineering Research Center, [3] UZ Leuven, Leuven, Belgium, Department of Dermatology, [4] UZ Leuven, Leuven, Belgium, Department of Rheumatology, [5] UZ Leuven, Leuven, Belgium, Department of Infectious Diseases.

Introduction : Despite the elevated risk for vaccine-preventable diseases and infection-related complications in patients with immune-mediated inflammatory diseases (IMID), vaccination coverage is still far from optimal. In 2015, we reported that only 32% of our patients with inflammatory bowel disease (IBD) were completely vaccinated according to guidelines.

Aim : We evaluated the evolution of vaccination coverage between 2015 and 2018 in IBD patients, and compared the current coverage with other IMID patients.

Methods : Between Aug 2018 and Oct 2018, the vaccination status of 829 consecutive IMID patients (43% male, median age 50 years) was collected at the outpatient clinics of a tertiary referral center (63% gastroenterology, 34% rheumatology, 3% dermatology). A one-page vaccination questionnaire was completed by the treating physician and reasons for non-vaccination were recorded. Missing data were added after contact with the general practitioner.

Results : Among IBD patients, vaccination rates had increased significantly from 2015 to 2018, namely 62% vs. 74% for pneumococci ($p<0.001$), 53% vs. 67% for hepatitis B ($p<0.001$), and 32% vs. 45% for all vaccines ($p<0.05$). One hundred and one patients were included in both IBD cohorts. Sixty-seven were not completely vaccinated according to guidelines in 2015 and 30 of them (45%) changed vaccination behavior in the last 3 years. Analysis of the current vaccination status demonstrated that overall 39% of the IMID patients were completely vaccinated according to guidelines. Vaccination rates were significantly greater in IMID patients followed at the gastroenterology department vs. patients followed at rheumatology, namely 74% vs. 36% for pneumococci ($p<0.001$), 67% vs. 45% for hepatitis B ($p<0.001$), 82% vs. 73% for tetanus ($p<0.01$), and 45% vs. 27% for complete vaccination according to guidelines ($p<0.001$). Regarding dermatology patients, IBD patients more frequently received a hepatitis B vaccination (67% vs. 46%, $p<0.05$). Scepticism (24% for influenza) and non-awareness (47% for pneumococci, 38% for hepatitis B and 42% for tetanus booster) were the most commonly reported reasons for non-vaccination.

Conclusions : Approximately 40% of all IMID patients were completely vaccinated according to guidelines. Although recent efforts on vaccination education in IBD patients have significantly improved vaccination rates, there is still need for awareness in both patients and health care professionals. 1 Coenen S., et al. Effects of Education and Information on Vaccination Behavior in Patients with Inflammatory Bowel Disease. *Inflamm Bowel Dis* 2017;23(2):318-24.

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DISTINCT AND COMMON GENE EXPRESSION PROFILES BETWEEN INFLAMED ILEUM AND COLON OF NEWLY DIAGNOSED CROHN'S DISEASE PATIENTS. S. Verstockt (1), F. Verdonck (1), B. Verstockt (2), M. Vancamelbeke (2), M. De Decker (3), E. Glorieus (4), V. Ballet (5), G. Van Assche (5), D. Laukens (4), M. Ferrante (2), F. Mana (3), M. De Vos (4), S. Vermeire (2), I. Cleynen (1) / [1] University of Leuven, Leuven, Belgium, Human Genetics, [2] University of Leuven, Leuven, Belgium, Translational Research Center for GastroIntestinal Disorders (TARGID), Department of Chronic Diseases, Metabolism and Ageing (CHROMETA), [3] University Hospitals Brussels, Belgium, Department of Gastroenterology, [4] University Hospital Gent, Gent, Belgium, Department of Gastroenterology, [5] University Hospitals Leuven, Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction : The clinical presentation of Crohn's disease (CD) is highly heterogeneous, and partly reflected by differences in disease location. The origin of this heterogeneous presentation is poorly understood.

Aim : We therefore aimed to characterize the molecular networks in inflamed tissue of CD patients with ileal and/or colonic disease location, and how they relate to control colon and ileum.

Methods : Inflamed colonic ($n=31$, 8 L2 + 23 L3) and ileal ($n=31$; 17 L1 + 14 L3) biopsies were collected from newly diagnosed CD patients across three Belgian IBD centres (PANTHER study B322201627472/S57662). Patients could be included if within 6 months after diagnosis, and if naïve for biologicals and immunosuppressives, and without previous IBD-related surgery. Colonic and ileal biopsies from respectively 36 and 14 non-IBD controls were used for comparison. All biopsies underwent single-end RNA sequencing, and data were corrected for age and gender in downstream analyses. Differential gene expression (fold change >2 , adjusted $p < 0.05$) was analysed using DESeq2, co-expression networks (correlation ≥ 0.55 , adjusted $p \leq 0.05$) with weighted gene co-expression network analysis (WGCNA), and pathways with IPA.

Results : As expected, we found many dysregulated genes between affected CD colon and control colon (1,031 genes), and between affected CD ileum and control ileum (1,227 genes), with an overlap of 581 genes. WGCNA identified 10 co-expression clusters. The number of genes in these clusters ranged from 180 to 1,611. Seven clusters were significantly correlated with our clinical traits (colonic CD or ileal CD compared to controls). More specifically, clusters I and IV were downregulated in both traits, while clusters II and III were upregulated in both. Cluster V was downregulated in ileal CD, and clusters VI and VII were respectively down- and upregulated in colonic CD. IPA analyses showed that cluster I was enriched in xenobiotic metabolism, cluster II in antigen presentation, cluster III in (a)granulocyte adhesion/diapedesis, cluster IV in AMPK signalling, cluster V in melatonin degradation, cluster VI in ERK5 signaling, and cluster VII in Th1 and Th2 activation. Interestingly, clusters I, II, V and VII were upregulated in ileal versus colonic location in controls, meaning that in control individuals, these clusters are more specific to the ileum than to the colon. Cluster VI

was downregulated in ileal versus colonic location in controls, meaning that this cluster is more specific to colon than to ileum in control individuals.

Conclusions : In this study, we identified both common and distinct gene expression profiles between inflamed ileum and inflamed colon of CD patients. While some gene networks were in general disease-related (eg. (a)granulocyte adhesion/diapedesis), others reflected an up- or downregulation of a location-specific signature in disease (eg. melatonin degradation), or even showed a loss of location-specific signature in disease (eg. xenobiotic metabolism).

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A POPULATION PHARMACOKINETIC MODEL TO SUPPORT THERAPEUTIC DRUG MONITORING DURING VEDOLIZUMAB THERAPY. E. Dreesen (1), B. Verstockt (2), M. Ferrante (3), S. Vermeire (3), A. Gils (1) / [1] University of Leuven, Leuven, Belgium, Department of Pharmaceutical and Pharmacological Sciences, [2] University of Leuven, Leuven, Belgium, Department of Chronic Diseases, Metabolism and Ageing, [3] University Hospitals Leuven, Belgium, Department of Gastroenterology and Hepatology.

Introduction : Patients with ulcerative colitis (UC) or Crohn's disease (CD) starting vedolizumab therapy can benefit from therapeutic drug monitoring.[1] A population pharmacokinetic model may support dose optimisation to improve attainment of predefined trough concentration targets.

Aim : To develop a population pharmacokinetic model to support therapeutic drug monitoring during vedolizumab therapy.

Methods : A total of 939 consecutive trough samples (from week 2 to week 30) of 178 patients (66 UC, 112 CD; excluding one patient with antibodies to vedolizumab) was used to develop a population pharmacokinetic model. We analysed these data under a known two-compartment model with parallel linear and nonlinear clearance by using informative prior distributions from the GEMINI population pharmacokinetic model to support estimation of pharmacokinetic parameters that were poorly supported by the current data (NONMEM 7.4 with \$PRIOR).[2] The classical stepwise covariate selection procedure was employed (forward $\alpha=0.01$, backward $\alpha=0.001$). Simulations were performed using Berkeley-Madonna 8.3.

Results : Our model with fully data-driven estimation of the linear clearance (CLL; 0.207 L/day [3%], typical value [% relative standard error]) and volume of distribution in the central compartment (V_c ; 4.62 L [9%]) showed good predictive capacity. Linear terminal elimination half-life of vedolizumab was 15.5 days (individual estimates ranged from 5.6 to 65.5 days), as compared to 13.9 days in GEMINI.[2] Lower albumin, mean platelet volume and haemoglobin, and higher C-reactive protein and fat-free mass were associated with higher CLL, thus predicting lower vedolizumab exposure. Prior anti-tumour necrosis factor-alpha therapy was not identified as a predictor of CLL. Furthermore, the CLL was not significantly different between patients with UC and CD. Still, 28% and 40% of the interindividual variability on CLL and V_c , respectively, remained unexplained. Patients with Mayo endoscopic sub-score ≤ 1 at week 14 had a lower vedolizumab CLL already at week 2 ($P = 0.009$). The vedolizumab CLL slightly decreased with time ($P = 0.028$). In addition, the cumulative area under the vedolizumab concentration-time curve from week 0 to week 14 was higher in patients with Mayo endoscopic sub-score ≤ 1 at w14 ($P = 0.001$). Although vedolizumab is characterised by nonlinear clearance, this only appeared to be relevant in the sub-therapeutic serum concentration range (<10.0 mg/L), providing additional motivation to target patients above the predefined ~ 14 mg/L trough concentration threshold during maintenance therapy. [1]

Conclusions : Our model demonstrates good predictive capacity and may be implemented in a therapeutic drug monitoring software tool to improve attainment of the exposure targets (trough concentrations and area under the curve) in individual patients with inflammatory bowel diseases. Bayesian updating of individuals' pharmacokinetic parameters, facilitated by a rapid assay, is recommended given the remaining large unexplained interindividual variability. References: [1] Dreesen E, Verstockt B, Bian S, et al. Evidence to Support Monitoring of Vedolizumab Trough Concentrations in Patients With Inflammatory Bowel Diseases. *Clin Gastroenterol Hepatol*. 2018. [Epub ahead of print] [2] Rosario M, Dirks NL, Gastonguay MR, et al. Population pharmacokinetics-pharmacodynamics of vedolizumab in patients with ulcerative colitis and Crohn's disease. *Aliment Pharmacol Ther*. 2015;42(2):188-202.

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SWITCH FROM ORIGINATOR INFLIXIMAB TO BIOSIMILAR CT-P13 IN INFLAMMATORY BOWEL DISEASE: A RETROSPECTIVE OBSERVATIONAL TWO-CENTER COHORT STUDY. J. Busschaert (1), N. Van Heddegem (2), D. Baert (2), P. Dewint (2), F. Baert (3) / [1] UZ Leuven, Leuven, Belgium, Gastroenterologie, [2] AZ Maria Middelaere, Ghent, Belgium, Gastroenterologie, [3] AZ Delta, Roeselare, Belgium, Gastroenterologie.

Introduction : Real life data on the switch from infliximab (IFX) originator to biosimilar in IBD are still scarce.

Aim : We studied efficacy and trough levels during and after switching from infliximab originator to biosimilar CT-P13, along with pro-active drug monitoring.

Methods : A retrospective, observational cohort study in 2 dedicated Belgian IBD centers was carried out between January 2017 and June 2018. All IBD patients responding to IFX originator maintenance therapy were switched to biosimilar CT-P13 after informed consent. The switch was mandatory, however in one center switching back was allowed. Proactive drug monitoring according to TAXIT algorithm was instituted at the same time. Disease activity (PRO2 for CD, Mayo for CU) was captured until the end of infliximab therapy or until the end of the study after 1-year follow-up. CRP, IFX trough levels (TL) (and if undetectable antibodies to infliximab (ATI)) were collected at the switch, 2 months, 6 months and at 1-year follow-up.

Results : A total of 135 patients were enrolled. Baseline characteristics: 54,9 % females, 99 CD, 36 UC, median duration of IFX therapy 7 years (range 2-16), 34% receiving combination therapy (28% on azathioprin, 6% on methotrexate). At baseline, IFX was stopped in 4 patients (3%) due to undetectable TL and high titers of ATI. Eighteen patients discontinued infliximab during the first year for different reasons: only 3 patients (2,22%) for inadequate disease control despite therapeutic TL; 6 for remission; 3 for adverse events (MS, lupus like syndrome, Ig A vasculitis); one 87-year old patient died (unrelated), 5 patients were lost to follow-up. All other patients experienced continued clinical, steroid free response during one year follow-up. No increase in CRP or thrombocytes was noted during one year follow-up. Applying the TAXIT protocol, the median interval between IFX infusions did not change before and after switch; 9 patients went from combination to monotherapy IFX (8 because of clinical remission and 1 patient on his request), in 1 patient on monotherapy methotrexate was associated because of inadequate symptom control. Median (+IQR) Remicade TL before was 5.2 (2,56-8,79) compared to CT-P13 first TL and one year 5,67 (3,36-9,03) and 5,31 (3,60-7,70) respectively. In the center where it is was allowed, 3 out of 49 patients (6,12%) switched back due to personal preference; no reverse switching occurred in the other center.

Conclusions : In our cohort mandatory switching from originator infliximab to biosimilar is cost-effective and doesn't lead to a higher rate of loss of response than the rate which can be anticipated in an infliximab originator treated IBD population. No immunogenicity was observed and pro-active drug monitoring confirmed TAXIT protocol as guidance for safety and preventing loss of response.

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- K01 -

CLINICAL PRE-TEST PROBABILITY FOR CELIAC DISEASE AND VALUE ADDED REPORTING OF IgA-TISSUE TRANSGLUTAMINASE ANTIBODIES IN THE PEDIATRIC SETTING. M. Cauchie (1), L. Bogaert (2), L. Van Hoovels (2), P. Vermeersch (3), G. De Hertogh (4), I. Hoffman (5), X. Bossuyt (3) / [1] Clinique de l'Europe site St-Michel, Etterbeek, Belgium, Department of Laboratory Medicine, [2] OLV Aalst, Aalst, Belgium, Department of Laboratory Medicine, [3] UZ Leuven, Leuven, Belgium, Department of Laboratory Medicine, [4] UZ Leuven, Leuven, Belgium, Department of Pathology, [5] UZ Leuven, Leuven, Belgium, Department of Paediatrics.

Introduction : In their most recent guidelines, the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) proposed the 'non-biopsy approach' for celiac disease (CD) diagnosis in children with clinical suspicion of CD: in presence of IgA-tissue transglutaminase (IgA-tTG) levels >10x the upper limit of normal (ULN), the presence of IgA endomysial antibodies (IgA-EMA), HLA-DQ2/DQ8 positivity and response to gluten-free diet (GFD) small bowel biopsies are not required for CD diagnosis.

Aim : The aim of this study was to improve serological evaluation of CD diagnosis and to determine whether the 'non-biopsy approach' of the ESPGHAN could obtain a post-test probability of >99% for CD diagnosis in children.

Methods : A total of 476 children (2-16y) who underwent endoscopy in a tertiary center were retrospectively included in this study. Among them, 69 children were diagnosed with CD. The presence of 16 predefined symptoms, 4 laboratory parameters, IgA-tTG, histological classification and response to GFD were registered for each patient.

Results : The prevalence of CD in our study population was 9.4%. Three symptoms (anorexia, abdominal distension and failure to thrive (FTT)) and 2 aberrant laboratory parameters (low ferritin level and elevated aspartate transaminase (AST)) were more prevalent in CD than in disease controls (i.e. non CD patients). Some combinations of symptoms/aberrant laboratory parameters showed a pre-test probability for CD of 100%. The likelihood ratio (LR) for 3 IgA-tTG level intervals were calculated in order to obtain post-test probabilities. The post-test probability for children with IgA-levels >10x ULN was 100%.

Conclusions : Our data confirm the excellent performance of the IgA-tTG assay in CD diagnosis. The ROC-curve analysis showed an area under the curve (AUC) of 0.98. Furthermore, the use of the ESPGHAN 'non-biopsy approach' allows a correct diagnosis of CD in symptomatic children with IgA-tTG levels >10x ULN. In our study population, this approach could reduce small bowel biopsies (and the associated risks), anesthesia and costs for the health care system in >80% of CD patients as 58 of 69 CD patients showed IgA-tTG levels > 10x ULN.

- K02 -

SWITCHING FROM INFLIXIMAB ORIGINATOR TO A BIOSIMILAR IS SAFE IN PAEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE WITHOUT AFFECTING EFFICACY, PHARMACOKINETICS AND IMMUNOGENICITY. K. van Hoeve (1), E. Dreesen (2), I. Hoffman (3), M. Ferrante (4), A. Gils (2), S. Vermeire (4) / [1] University Hospitals Leuven, Leuven, Belgium, Department of Paediatric gastroenterology & Hepatology & Nutrition, [2] Catholic University of Leuven (KU Leuven), Belgium, Laboratory for Therapeutic and Diagnostic Antibodies, Department of Pharmaceutical and Pharmacological Sciences, [3] University Hospitals Leuven, Belgium, Department of Paediatric gastroenterology & Hepatology & Nutrition, [4] University Hospitals Leuven, Belgium, Department of Gastroenterology & Hepatology.

Introduction : Rising evidence demonstrates no differences in efficacy and safety between infliximab (IFX) originator and IFX biosimilar CT-P13 in inflammatory bowel diseases (IBD). However, most data are derived from adult patients and data on pharmacokinetics are limited.

Aim : The aim of this study was to evaluate the long-term changes in IFX trough levels (TL), immunogenicity and remission rates after switching from the IFX originator to the biosimilar CT-P13 in pediatric IBD patients during maintenance therapy.

Methods : In this single-centre study, all children with Crohn's disease (CD) and ulcerative colitis (UC) receiving maintenance IFX therapy between July 2017 and January 2018 were included. Eligible subjects were all patients, who had been receiving the IFX originator for at least four months (in order to receive at least one maintenance infusion of the IFX originator before switch). The switch to CT-P13 was imposed by the hospital for all patients regardless of the indication as from January 2018. Demographics, disease activity indices, IFX TL and antibodies to IFX (using Ridascreen IFX Monitoring ELISA) were collected from 6 months before (baseline) till 6 months after switch. Clinical remission was defined as PUCAI/PCDAI <10 and biological remission as CRP ≤5 mg/L and ESR ≤20 mm/h. For paired comparison of data obtained at the different timepoints, a Wilcoxon signed-rank sum test and a McNemar test were used for continuous and dichotomous variables, respectively. All data are presented as median [interquartile range]. Alpha was set at 0.05.

Results : A total of 47 children received maintenance therapy with the IFX originator at our centre. Forty-two children (26 CD and 16 UC), were eligible for the study as 3 patients were transferred to the adult department and 2 patients stopped IFX just before the switch (due to loss of response or delayed infusion reaction). Included patients had a median duration on IFX originator of 13.5 [6.8-35.5] months prior to switch. No significant changes in IFX TL occurred after switching to CT-P13. The median baseline IFX TL was 5.7 [3.8-9.3] µg/mL versus 6.5 [3.9-8.6] µg/mL at month 6 after switching to CT-P13 (p=0.90). The cumulative IFX dose administered over a 6 month period was not significantly different before switch (36.6 [24.0-53.3] mg/kg) compared to after switch (35.8 [26.7-55.6] mg/kg; p=0.21). Antibodies to IFX appeared only in 1 patient after switching to CT-P13. The proportion of patients in clinical and/or biological remission did not significantly change after switch (all p> 0.05). No significant changes were observed in C-reactive protein, erythrocyte sedimentation rate, albumin or weight and body mass index (expressed as z-score) after switch. No new safety signals were observed after switching to CT-P13.

Conclusions : Paediatric IBD patients on IFX originator can be successfully switched during maintenance to CT-P13 without affecting efficacy, pharmacokinetics, immunogenicity and safety.

- K03 -

EFFICACY AND SAFETY OF BISMUTH BASED QUADRUPLE THERAPY FOR HELICOBACTER PYLORI ERADICATION IN CHILDREN: AN INTERIM ANALYSIS. K. Kotilea (1), D. Nguyen (2), A. Salame (1), T. Mahler (1), V. Miendje Deyi (3), P. Bontems (2), S. Cadranel (2) / [1] HUDERF, Brussels, Belgium, Pediatric Gastroenterology, Hepatology and Obesity, [2] HUDERF, Brussels, Belgium, Paediatric Gastroenterology, Hepatology and Obesity, [3] LHUB-ULB, Brussels, Belgium, Bacteriology.

Introduction : Helicobacter pylori (H. pylori) infection causes chronic gastritis, peptic ulcer disease and is involved in the development of gastric cancer. An eradication treatment is currently indicated in case of peptic ulcer disease, of refractory iron deficiency anaemia of chronic idiopathic thrombocytopenic purpura and can be considered in case of non-ulcer dyspepsia (symptoms similar to Rome III criteria for functional dyspepsia) after deliberations with the patient and the family. Due to the growing resistance of H. Pylori strains to antibiotics and the decreasing efficacy of classical triple therapy, bismuth-based quadruple therapies are proposed as first-line in adults while recent data on their efficacy and tolerability are lacking in children.

Aim : To evaluate the efficacy and safety of colloidal bismuth sub-citrate (CBS) as adjunctive therapy to a combination of esomeprazole (ESO), amoxicillin (AMO) and metronidazole (MET) for 10 days for Helicobacter pylori (H. pylori) eradication in children.

Methods : Monocentric, open-label, prospective, interventional single arm clinical trial to assess the safety and efficacy of a 10 days CBS as an adjunctive therapy in combination with ESO, AMO and MET in children aged 6 to 17 years with H. pylori infection. The study is registered in ClinicalTrials.gov with identifier: NCT03299725. The study is carried out on consecutive patients with upper gastrointestinal symptoms and H. pylori infection confirmed by histology and culture of gastric biopsies. The outcome of the treatment was evaluated using a 13C-urea breath test performed 8-10 weeks post therapy. Compliance for CBS was evaluated by counting the remaining pills while compliance for ESO, AMO and MET as well as adverse events were evaluated by a paper journal filled by the parents and patient.

Results : After one year, we run an interim analysis. A total of 22 consecutive patients fulfilling the inclusion criteria were enrolled into this study. Out of them, 19 have already completed the follow-up. In this cohort, 4 patients (21%) had a prior history of medication to treat H. pylori. Antimicrobial susceptibility testing showed that 5 of them were infected by a strain resistant to MET and 3 of them by a strain resistant to both MET and Clarithromycin (CLA). In the intention - to- treat population, eradication was achieved in all 19/19 patients (95%CI: 83,2% -100%). At least one adverse event possibly related to the treatment was reported by 11 children (57,9%), mostly mild (metallic taste, dark stool, nausea, vomiting, abdominal pain, headache). Only one patient had to stop at day 8 due to an urticaria rash and was treated for the two remaining treatment days by an ESO-MET-CLA scheme. Skin prick tests were performed in this child and did not prove hypersensitivity for AMO MET or CBS (oral challenges pending). Compliance was very satisfactory with 13 patients taking >90% of the treatment (68,4 %), 5 patients taking 80-90% of the treatment (26,3%) and only one patient <80% (5,2%). This last patient did not fulfill compliance for CBS (half the dose received) but was fully adherent to the rest of the treatment.

Conclusions : CBS as adjunctive therapy to a combination of ESO, AMO and MET given for 10 days for H. pylori eradication in children seems to be a safe and very effective solution, especially for resistant strains and previously treated patients. Larger number of subjects and a multicentric design is necessary to validate this hypothesis.

- K04 -

EVALUATION OF COMPLIANCE IN YOUNG TRANSPLANT PATIENTS. R. Weyts (1), A. Geerts (1), R. De Bruyne (1), X. Rogiers (1), A. Vanlander (1), C. Poppe (1) / [1] Universitair ziekenhuis Gent, Belgium, Transplantatiecentrum.

Introduction : Compliance problems in transplant patients is a significant factor. Within transplant patients in transition there are even more risks. These risks are caused by their lifestyle and the movement from paediatrics to adults. Compliance problems cause a higher risk for late acute rejection and graft losses. Next to personal costs, social costs of health care are increasing due to the inefficient use of sources and the shortage of donors.

Aim : We studied the compliance after transplantation in young people in transition between the ages of 12 and 25. This age range includes the phase in which young people have to make the transition from paediatrics to adults. We aimed to identify the difficulties in the achievement of good compliance and define suggestions for improvement of compliance behaviour.

Methods : Fifteen respondents from the University Hospital Ghent were interviewed in qualitative in-depth interviews. The composition of the interviews is based on Mortelmans' (2013) handbook about qualitative research and was reviewed by professors in the research field and transplantcenter. The interviews were conducted by a researcher who is also a transplant patient.

Results : The results are shown in three components: adherence, defining difficulties and suggestions for improvement. Adherence: Fourteen respondents indicated that they sometimes forgot their medication and each respondent believed that there was room for improvement within the adjustments in lifestyle. Defining difficulties: The determining factors in the process of adherence appeared dependent on the time after the transplant. The doctor-patient relationship and support from the parents have the greatest influence closely after the transplant surgery. Next were impact on daily life and physical consequences also difficulties to reach a better adherence. After the adjustment period, the need for making own decisions and disease perception were more decisive factors. A factor found to have an important influence on patient adherence independently of the time after transplantation is self-image. Suggestions for improvement: Next to a personal connection with their doctor, patients want an open communication. A clear message in which the doctor tells them what is important and for what reasons. In this way, they feel able to ask all kind of questions and they can make more personal decisions. In addition, they show need for more knowledge about the transplantation, medication and side effects in the form of information sessions by doctors and testimonials of patients. This stays important on the long run when the patient seems adjusted to his transplanted situation, to keep the awareness of the importance of a good adherence alive. Finally, other recommendations to improve their compliance behaviour were the use of alarms, medication boxes and phone applications to reduce the practical influence. In addition, they stressed a context of concrete goal setting and consciously reflecting with them on the long-term consequences. This was advised in order to facilitate the adaptations to the lifestyle. Also, it was recommended to provide psychological help if needed and to stimulate them to talk openly about adherence with friends or other patients. Doing things to optimize the self-image were always seen as important.

Conclusions : First, compliance problems in transplant patients are a significant factor. Second, we conclude that based on qualitative in-depth interviews, adherence to therapy among young patients in transition, can be improved by investing in the personal relationship between patient and caregivers. Hence, the knowledge about the transplantation and the reason for the lifestyle changes can be discussed and be better understood. Furthermore, talking about the transplant condition and difficulties with compliance with caregivers, family and friends can improve self-image and compliance behaviour.

- K05 -

LONG-TERM OUTCOME OF CHILDREN WITH INFLAMMATORY BOWEL DISEASE TREATED WITH OF IMMUNOMODULATORS. K. van Hove (1), I. Hoffman (1), M. Ferrante (2), S. Vermeire (2) / [1] University Hospitals Leuven, Belgium, Department of Paediatric gastroenterology & Hepatology & Nutrition, [2] University Hospitals Leuven, Belgium, Department of Gastroenterology & Hepatology.

Introduction : In the era where new powerful biologicals are entering the market, the place of conventional immunomodulators (IMM) in treatment of paediatric inflammatory bowel disease (IBD) is questioned.

Aim : We studied the long-term outcome of paediatric IBD patients receiving conventional therapy.

Methods : All children with Crohn's disease (CD) or ulcerative colitis (UC) followed at our centre between July 2008 and July 2018 were retrospectively included. Only children receiving conventional therapy including mesalazine, steroids and IMM (thiopurine, methotrexate) at start were studied. Patients requiring rescue therapy (either biologics or surgery) around diagnosis or with a follow-up (FU) <6 months were excluded. The primary outcome of interest was steroid-free clinical remission without need for rescue therapy at 6 and 12 months after diagnosis and at last FU visit. Cox proportional hazard modelling was performed (Hazard risk: HR (95% CI) to determine variables associated with outcomes.

Results : A total of 221 patients (149 CD and 72 UC; 49% male) with a median age at diagnosis of 12 [IQR: 10-14] years were included. Median disease activity score (PCDAI and PUCAI) at diagnosis was 30 [IQR: 22-43] and 50 [IQR: 30-60] for CD and UC, respectively. IMM were started in 194 (88%) patients after a median duration of 1 [IQR: 0-3] month. We excluded 45 (20%) patients due to insufficient FU (n=21), need of biologics (n=22) or surgery around diagnosis (n=2). Reason to start rescue therapy around diagnosis was steroid resistant patients (n=10), peri-anal Crohn's disease (n=7), severe disease at presentation associated with a TPMT mutation (n=5), and presentation with an ileocaecal

abscess or intestinal obstruction with stricture requiring surgery (n=2). A total of 176 patients were eligible for the study, with a median FU duration of 5 [IQR: 2-8] years. Steroid-free clinical remission rates decreased from 80% at month 6, and 58% at month 12, to 32% at last FU visit. The likelihood of remaining free of rescue therapy was 53% and 72% at 1 year and 27% and 31% at 5 years for CD and UC patients, respectively. For CD patients, higher CRP [HR 1.007 (1.002-1.011), p=0.002], lower albumin [HR 1.045 (1.008-1.080), p=0.016] and growth failure [HR 1.206 (1.011-1.362), p=0.040] at diagnosis were associated with an increased risk of need of rescue therapy. For UC patients, higher PUCAI score at diagnosis [HR 1.037 (1.009-1.065), p=0.008] was determined as a risk factor for rescue therapy.

Conclusions : These real-life data in paediatric IBD show that only 32% of children remain free of biologic or surgery 5-years after diagnosis. Especially children with a high disease burden at diagnosis as witnessed by higher CRP, lower albumin and growth failure for CD and higher PUCAI score for UC were more likely to fail conventional therapy. This type of risk stratification algorithms will help to determine which patients will benefit from accelerated step-up therapy.

- K06 -

FATIGUE IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE: A PROSPECTIVE OBSERVATIONAL STUDY OF A PATIENT AND CONTROL GROUP. L. Le Roy (1), L. Braeckveldt (1), S. Verstraete (1), S. Vande Velde (1), E. Van de Vijver (2) / [1] Ghent University Hospital, Ghent, Belgium, Pediatric Gastroenterology, [2] Antwerp University Hospital, Edegem, Belgium, Pediatric Gastroenterology.

Introduction : Fatigue is a common symptom among patients with inflammatory bowel disease (IBD). However, the presence of fatigue in children with IBD has not yet been extensively studied.

Aim : We aimed to assess fatigue and physical capacity amongst children with IBD compared to healthy peers and to evaluate its correlation with disease activity scores, faecal calprotectin level and Quality of Life.

Methods : We compared a group of 70 IBD children aged 7 to 18 years old from University hospital Ghent and Antwerp (UZG and UZA) with 66 age matched children. The patients and controls and one of the parents filled in the Dutch Multidimensional Fatigue Questionnaire to assess the degree of general fatigue, sleep/rest fatigue and cognitive fatigue. Patients and controls performed the six-minute walk test (6MWT). Only patients completed the Impact-III (HR) Questionnaire and had faecal calprotectine levels, PCDAI (pediatric crohn's disease activity index) and PUCAI ("pediatric ulcerative colitis activity index) scores measured.

Results : The proxy-reported total fatigue scores were significantly higher than the self-reported scores (p=0,015) from both IBD patients and healthy peers. The PedsQL scores of the children with IBD were significantly lower (higher level of fatigue) regarding general fatigue (p<0,000) and sleep/rest fatigue (p=0,015). Cognitive fatigue was not different between IBD children and healthy controls (p=0,121). 6MWD was comparable between IBD group and healthy controls (p=0,071). Within the IBD group, there was no significant difference in PedsQL fatigue scores and IMPACT scores between CD and CU (P=0,518). The impact score (meaning high impact of the disease on their life quality) was significantly correlated with the self-reported total fatigue score and with general fatigue. No significant correlation was found between the 6MWT and the impact score (p=0,816), or the general fatigue (p=0,751) in the overall IBD group. CD patients with a normal level of calprotectine (<250 µg/g) reported a higher PedsQL score (lower level of fatigue) and a lower impact III score (higher quality of life) than children with a high calprotectine level (>1500µg/g) (P=0,048 and P=0,049). This was not seen in children with CU. Elevated (10-35) PUCAI scores are correlated with a higher fatigue score, PCDAI scores not.

Conclusions : Children with IBD report more fatigue than their healthy peers, especially general fatigue. A high level of fatigue is correlated with a low quality of life in both CD and CU. More fatigue in IBD is not a consequence of decreased physical fitness, since 6MWD results were comparable between IBD patients and healthy controls. Calprotectine level is in CD patients linked to fatigue, but not in UC patients. Disease activity scores show conflicting results.

- K07 -

LOW EFFICACY OF SECOND LINE TREATMENTS FOR H. PYLORI ERADICATION IN CHILDREN. K. Kotilea (1), A. Salame (2), E. Lenga (2), T. Mahler (2), V. Miendje-Deyi (3), M. Urbanowicz (4), S. Cadranel (2), P. Bontems (2) / [1] HUDERF, Brussels, Belgium, Pediatric Gastroenterology, [2] HUDERF, Brussels, Belgium, Paediatric Gastroenterology, Hepatology and Obesity, [3] LHUB-ULB, Brussels, Belgium, Bacteriology, [4] CHU Brugmann, Brussels, Belgium, Pathology.

Introduction : Few data address the question of the efficacy of rescue treatments for Helicobacter pylori (H. pylori) infection in children.

Aim : To evaluate the efficacy of second line eradication treatments for H. pylori infection in our pediatric center.

Methods : Open, single - center, retrospective study. We included all children aged 2-17 years who had previously received one treatment scheme for eradication that failed. Persistence of infection after first treatment was confirmed

either by 13C-urea breath test (UBT) or by histology and/or H. pylori culture of gastric biopsies. A second line eradication scheme, either a sequential treatment either a triple therapy (tailored when secondary antimicrobial susceptibility was available) with duration and dosage in accordance with local treatment protocols (which were changing over time), was proposed. Treatment outcome was evaluated by 13C-UBT.

Results : Between Nov 2011 and Nov 2018, 477 children received a first line treatment and 88 met the inclusion criteria (46 identified by UBT with eradication failure after a first line treatment and 42 by per-endoscopic gastric biopsies). A second line treatment was prescribed in 59/88 (median age 10.8 y). Eradication was achieved in only 35/59 children (59% - 95%CI 47%-72%) in intention-to-treat analysis and in 35/52 of those who performed the post-treatment evaluation (67% (95% CI 55%-80%). However, eradication rate was excellent (33/35 - 94% (95%CI 87%-100%) when compliance to the rescue treatment was > 90%. In monovariate analysis, neither the type of treatment, nor drugs dosage nor duration of treatment nor time period significantly affect the outcome. No difference in eradication rates was observed also between the tailored and the empiric treatments (16/21 vs 19/31, OR 2.02 95%CI 0.59-6.96 p = 0.27). The only factors that were significantly associated to a successful eradication were compliance >90% to treatment (OR 123.75, 95%CI 15.88 to 964, p<0,0001) and the absence of adverse events during treatment (OR 5.24 95%CI 1.48 to 18.53, p=0.01).

Conclusions : The efficacy of second line treatment for H. pylori eradication is low in children unless an excellent compliance can be achieved. No eradication attempt should be initiated when there is a doubt about strict adherence to treatment or tolerance. Low compliance is the factor that influences the most treatment outcome whereas drugs dosage or duration of treatment or a tailored scheme to susceptibility profile have less influence.

- K08 -

THE PRESENCE OF SERUM AUTOANTIBODIES AND DONOR-SPECIFIC ANTI-HLA ANTIBODIES IN PEDIATRIC LIVER TRANSPLANT RECIPIENTS IS ASSOCIATED WITH HISTOLOGICAL AND BIOCHEMICAL PARAMETERS OF GRAFT DYSFUNCTION. E. Saelens (1), C. Bonroy (2), S. Van Biervliet (3), S. Vande Velde (3), M. Van Winckel (3), X. Rogiers (4), A. Vanlander (4), R. De Bruyne (3) / [1] Ghent University, Ghent, Belgium, Faculty of Medicine and Health Sciences, [2] Ghent University Hospital, Ghent, Belgium, Department of Clinical Biology, [3] Ghent University Hospital, Ghent, Belgium, Department of pediatric gastroenterology, hepatology and nutrition, [4] Ghent University Hospital, Ghent, Belgium, Department of Hepatobiliary Surgery.

Introduction : Serum autoantibodies (AAb) as well as donor-specific anti-HLA Ab (DSA) are frequently present in pediatric liver transplant (LT) recipients. Their clinical significance remains incompletely understood when encountered outside the context of de novo autoimmune hepatitis (AIH).

Aim : To study the prevalence of serum AAb and DSA in pediatric LT recipients under follow-up at Ghent University Hospital and investigate their correlation with patient characteristics and clinical outcome in terms of histological and biochemical parameters.

Methods : Based on electronic patient data, we retrospectively collected the data on AAb (antinuclear factor, ANF; anti-smooth muscle Ab, ASMA; anti-soluble liver antigen Ab; anti-liver cytosol type 1 Ab; anti-liver kidney microsomal Ab) and DSA in 62 pediatric LT recipients (median age 3,8 y; range 0,1-17,1 y; 37 male) under follow-up at Ghent University Hospital between January 2007 and February 2018. The patient characteristics (age, sex, age at LT, time of follow-up, LT indication, donor type and age, need for retransplant or death), need for liver biopsy (LB) and number of LB, histological findings (acute cellular rejection; chronic rejection; histological signs suggestive of biliary obstruction; de novo AIH; idiopathic post transplant hepatitis (IPTH); aspecific alterations and steatosis) and biochemical parameters (Alkaline Phosphatase, AP; ALT; AST; γ -GT; total and direct bilirubin; albumin; thrombocyte count; Immunoglobulin G; EBV and CMV DNA) were registered at several time points (year 1, 3, 5, 10 and 15) post LT. Statistical analysis was performed using SPSS Statistics (version 25). The following tests were used: Chi2-test or Fisher's exact test (categorical variables), Mann-Whitney U test (continuous variables), Mc Nemar test (paired tests).

Results : AAb were detected in 27 (43,3%) patients, with ANF being the most frequently encountered AAb in 15 (24,2%) patients followed by ASMA in 13 (21%) patients. There was a positive correlation between AAb positivity and female gender (p=0,032) and cadaveric LT (p=0,006). In 54 patients at least one liver biopsy was performed during their post-transplant course. Acute cellular rejection was present in 20 (32%), chronic rejection in 7 (11%), histological signs of biliary obstruction in 16 (25%), de novo AIH in 4 (6,5%), aspecific histological changes in 25 (40%), IPTH in 5 (8,1%) and steatosis in 12 (19%) patients. Patients with positive AAb underwent a higher number of LB during their follow-up (p<0,001) and in the absence of de novo AIH, an association was found with the presence of aspecific histologic alterations (p=0,032). Outside the context of de novo AIH, positive AAb were associated with increased AP (p<0,001), ALT (p<0,001), AST (p<0,001), γ -GT (p=0,001), IgG (p=0,007) and decreased albumin (p=0,029). 14 out of 50 patients were DSA positive (all anti-HLA class II). DSA positivity was associated with acute cellular rejection (p=0,019), increased direct bilirubin (p=0,033) and γ -GT (p<0,001).

Conclusions : The presence of AAb in the absence of de novo AIH as well as DSA positivity is associated with histological and biochemical parameters of graft dysfunction. Larger prospective studies are warranted to further investigate the causal relationships between AAb and DSA development and outcome parameters post pediatric LT.

NON-INVASIVE ASSESSMENT OF LIVER ABNORMALITIES IN PEDIATRIC FONTAN PATIENTS. R. De Bruyne (1), K. Vandekerckhove (2), F. Hendrickx (3), H. Van Overschelde (4), C. Vande Walle (5), K. De Groote (2), J. Panzer (2), D. De Wolf (2), S. Van Biervliet (1), T. Bové (6), K. François (6) / [1] Ghent University Hospital, Ghent, Belgium, Department of pediatric gastroenterology, hepatology and nutrition, [2] Ghent University Hospital, Ghent, Belgium, Department of pediatric cardiology, [3] Ghent University, Ghent, Belgium, Faculty of Medicine and Health Sciences, [4] Ghent University, Ghent, Belgium, Faculty of Medicine and Health Sciences, [5] Ghent University Hospital, Ghent, Belgium, Department of pediatric radiology, [6] Ghent University Hospital, Ghent, Belgium, Department of cardiothoracic surgery.

Introduction : The Fontan procedure remains the definite surgical palliation in patients with complex congenital heart disease and single ventricle physiology. Liver abnormalities are well-known among long-term survivors of Fontan palliation, pediatric data however are scarce.

Aim : We aimed to assess the prevalence and degree of liver abnormalities in pediatric Fontan patients through non-invasive investigations suitable for longitudinal follow-up.

Methods : The study population consisted of 35 Fontan patients (median age 11,8 y; range 5,2-16,6 y; 27 male). The median (range) time since Fontan was 3,29 y (2,17-6,98). Each child underwent a liver ultrasound scoring for nodularity, coarsened echotexture, ascites, collateral circulation; liver and spleen size were evaluated through US midclavicular liver diameter and splenic length respectively. Via Doppler US, the diameters of inferior vena cava (IVC) and portal vein (PV) in in- and expiration together with the IVC collapsibility index (IVCCI) were measured. The pulsatility ratio (PR) of the PV and hepatic vein (HV) was calculated as well as the damping index (DI) as an alternative for the PV pulsatility index (PI). The resistance index (RI) of the PV, hepatic artery (HA) and superior mesenteric artery (SMA) was examined. Fibroscan (Echosens) was used to perform transient elastography (TE). The fibroscan results were compared with measurements in a pediatric healthy control population consisting of 73 children with a median (range) age of 10,52 y (5,67-18,33) (38 male). A blood test was performed with analysis of the following parameters: AST, ALT, γ GT, Alk Phos, bilirubin, total protein, albumin, alpha-foetoprotein, platelet count, cholesterol and Apo-lipoprotein A1. The fibrosis scores APRI, FIB4 and Forns were calculated. The study was approved by the Ethics Committee of Ghent University Hospital. Statistical analysis was performed with SPSS Statistics version 24.0.

Results : Liver US showed nodularity of the liver parenchyma in 2 patients and irregularity of the liver surface in 2 other patients. Hepatomegaly was present on US in 32% of patients, splenomegaly in 15%. PV mean flow velocity was < 15 cm/sec in 19 (54%) of patients, correlating with portal hypertension (1). Mean IVCCI (13,7% \pm 9%) was significantly decreased compared to normal values ($p < 0,001$). 22 patients (63%) showed IVCCI values below 17%, indicative of venous congestion (2). HA RI and SMA RI were inversely correlated with time post Fontan ($p < 0,05$; $r^2 = -0,369$ and $r^2 = -0,365$ resp.). Liver stiffness was significantly increased in the Fontan group compared to controls, with a median (range) of 12,6 kPa (6,6-25,7) versus 4,6 kPa (2-9,5) ($p < 0,001$). TE values were already increased shortly after total cavopulmonary connection and did not tend to increase with time post Fontan. AST, ALT, γ GT and direct bilirubin were abnormally increased in respectively 12 (34%), 5 (14%), 24 (69%) and 7 (20%), whilst platelet count was decreased in 7 (20%) of the patients. For the 3 fibrosis scores, only one patient exceeded the cut-off value for METAVIR F2.

Conclusions : Liver abnormalities are frequently observed in pediatric Fontan patients and seem to be mostly correlated with hepatic congestion. The used non-invasive investigations were not able to confirm liver fibrosis or differentiate hepatic congestion from fibrosis. Based on our findings, we propose future prospective follow-up with serial measurements of lab values (ALT, γ GT, direct bilirubin, alpha-foetoprotein, platelet count as well as clotting profile), US and Doppler parameters (liver and spleen morphology, IVCCI, PV flow velocities, HA RI, SMA RI as well as PV pulsatility index) and TE to further elucidate this problem. The quest for reliable, readily applicable and accurate non-invasive techniques to assess liver fibrosis in children remains a major topic for future research. (1) Zironi G et al. J Hepatol 1992;16(3):298-303 (2) Kutty S et al, J Am Soc Echocardiogr 2014; 27(2):155-62

BELGIAN WORKING GROUP ON PROCTOLOGY

- M01 -

FISTULA-TRACT LASER CLOSURE (FILACTM) AS A LAST RESORT FOR TREATMENT-RESISTANT PERIANAL FISTULA: CASE SERIES AND REVIEW OF THE LITERATURE. N. De Hous (1), C. de Gheldere (2), S. Van Den Broeck (3), N. Komen (3) / [1] Universiteit Antwerpen / Antwerp University Hospital, WILRIJK (Antwerpen), Belgium, Abdominal Surgery, [2] Heilig Hart Ziekenhuis, Lier, Belgium, General and abdominal surgery, [3] Universiteit Antwerpen / Antwerp University Hospital, WILRIJK (Antwerpen), Belgium, Abdominal surgery.

Introduction : Complex, treatment-resistant perianal fistula remains a surgical challenge as multiple interventions are often needed to achieve closure. Fistula-tract Laser Closure (FiLaCTM) is a new, simple and minimally invasive sphincter-preserving treatment for perianal fistula with a healing rate ranging from 65 to 80%.

Aim : The objective of this study is to introduce FiLaCTM as a valuable treatment option in these patients.

Methods : Between November 2016 and December 2018, a consecutive series of patients with complex, treatment-resistant perianal fistulas were included. The surgical technique consisted of proper drainage of the fistula, blind cauterization of the tract with the radial-emitting laser probe and closure of the internal orifice. Fistula closure was defined as closure of the external opening and absence of symptoms.

Results : 11 patients with a median age of 51 years (range 30-63) were included. Of these patients, 8 had cryptoglandular fistulas and 3 suffered from Crohn's disease. Each patient had a history of multiple, failed surgical interventions (median 5, range 3-13). At a median follow-up length of 9 months (range 4-26), 8 of 11 (73%) fistulas were closed after one or more FiLaCTM sessions. The fistula persisted or recurred in 3 patients.

Conclusions : FiLaCTM seems a good option in the management of treatment-resistant perianal fistula, especially because the procedure can easily be repeated without extensive dissection or creating open wounds. Larger studies in trial setting are needed to further investigate the efficacy of FiLaCTM in these patients.

- M02 -

RADIO FREQUENCY ABLATION (RAFAELO PROCEDURE) AS TREATMENT FOR HAEMORRHOIDS, A PILOT STUDY. M. De Visschere (1), D. De Looze (2), D. Van de Putte (1), P. Pattyn (1) / [1] UZ Gent, Gent, Belgium, Gastro-intestinal Surgery, [2] UZ Gent, Gent, Belgium, Gastroenterology.

Introduction : The Rafaelo procedure involves Radio Frequency Ablation of the haemorrhoids under local anesthesia.

Aim : Evaluation of the safety and effectiveness of the Rafaelo procedure as treatment for haemorrhoids.

Methods : From March 2017 till December 2018, 9 patients were included in this prospective study. The Rafaelo procedure was performed to treat the haemorrhoids. The procedure involves Radio Frequency Ablation of the haemorrhoids by use of the EVRF device, F Care Systems, under local anesthesia. We analyzed the adverse events, postoperative complications and outcome of the procedure. Pre- per and postoperative data were prospectively collected.

Results : 9 patients were included (mean age 51). All patients were treated for bleeding haemorrhoids with prolapse grade II (7 patients, 78%) and grade III (2 patients, 22%). Our mean operation time was 30 minutes, due to the fact that this procedure was totally new for the team, so we had to overcome the learning curve. For that reason we did the first two cases under sedation (midazolam+remifentanyl). For the next 7 cases we used local anesthesia. 5 patients experienced the procedure as comfortable with only little pain. For two patients we had to add sedation, because the placement of the proctoscope was already painful. Two or three pillars were treated per patient. There were no complications during the procedure nor early postop complications. The reported pain postoperatively was diverse with a range of VAS score from 2 to 9 (average highest score was 4.2). Patients took their painkillers for 11 days on average (range 0 days to 3 weeks). Most patients were free of pain after 2 weeks, only 3 felt some pain for about 1 month. (Range 4 days-30days) At follow up (mean 9months), all patients had a very good improvement of their bleeding complaints. 6 patients had no longer blood loss at all, three still had a few times a month some blood loss. No patient developed stenosis nor other complications.

Conclusions : The Rafaelo procedure is a safe and effective procedure for the treatment of haemorrhoids, especially for complaints of blood loss. One-year follow up results are promising. Comparative prospective studies are needed to determine the place of the Rafaelo procedure amongst classical haemorrhoidectomy, non-incisional haemorrhoidal techniques (HAL-RAR) and non-surgical interventions.

BELGIAN GROUP FOR DIGESTIVE ONCOLOGY (BGDO)

- 001 -

COMBINING BASELINE 18F-FDG PET/CT-BASED METABOLICALLY ACTIVE TUMOR VOLUME AND EARLY DETECTION OF NON-RESPONSE SIGNIFICANTLY IMPROVES OUTCOME PREDICTION IN CHEMOREFRACTORY METASTATIC COLORECTAL CANCER.

E. Woff (1), A. Hendlisz (2), L. Ameye (3), T. Guiot (1), M. Paesmans (3), A. Deleporte (2), K. Geboes (4), T. Delaunoit (5), G. Demolin (6), M. Peeters (7), L. D'hondt (8), J. Janssens (9), J. Carrasco (10), S. Holbrechts (11), J. Van Laethem (12), P. Flamen (1) / [1] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, Nuclear Medicine, [2] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, Medical Oncology, [3] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, Data centre, [4] Universitair Ziekenhuis Ghent, Ghent, Belgium, Digestive Oncology, [5] Hôpital de Jolimont, Haine-Saint-Paul, Belgium, Oncology Department, [6] Centre Hospitalier Chrétien St-Joseph, Liège, Belgium, Gastroenterology Department, [7] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Oncology Department, [8] CHU-UCL-Namur site Godinne, Yvoir, Belgium, Oncology Department, [9] AZ TURNHOUT, Turnhout, Belgium, Gastroenterology Department, [10] Grand Hôpital de Charleroi, Hôpital Saint-Joseph, Gilly, Belgium, Oncology Department, [11] CHU Ambroise Paré, Mons, Belgium, Medical Oncology, [12] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Digestive Oncology.

Introduction : Metastatic colorectal cancer (mCRC) has a poor prognosis despite important improvements in its management. However, strong variations in survival among patients are nevertheless noted at least partially related to differences in disease burden and the presence of treatment refractory lesions. New prognostic/predictive biomarkers are urgently needed to better identify patients at high/low risk of early death. New 18F-FDG PET/CT-based biomarkers developed recently allow the assessment of whole-body metabolically active tumor volume (WB-MATV) and rapid identification of treatment resistance.

Aim : This prospective study aimed to evaluate if the early PET response (Response vs. Non-Response) adds a significant prognostic value to baseline WB-MATV along with clinical factors on overall and progression-free survival (OS/PFS) in a large cohort of chemorefractory mCRC patients treated with multikinase inhibitors.

Methods : A total of 224 patients with unresectable chemorefractory mCRC were enrolled in two prospective multicenter non-randomized clinical trials investigating new targeted agents: combined sorafenib/capecitabine (EudraCT number: 2010-023695-91) and regorafenib (EudraCT number: 2012-005655-16). Standardized baseline and early 18F-FDG PET/CT scans were performed within 2 weeks before treatment and 2-3 weeks after the beginning of the therapy, respectively. 216 patients were considered suitable for an intention-to-treat analysis. Non-Responder patient was identified when at least one target lesion showed no significant decrease of SUVmax (<15%). WB-MATV optimal cutoff of 100 cm³ for prediction of OS/PFS was determined by Contal and O'Quigley's method. Univariate analyses for OS/PFS were performed to assess the prognostic values of baseline WB-MATV/early PET response and multivariate analyses for OS/PFS to assess their prognostic independency along with well-known clinical factors (i.e. age, gender, BMI, ECOG performance status, time since diagnosis, previous use of bevacizumab, KRAS mutation, and use of sorafenib vs. regorafenib).

Results : Univariate analyses showed that both WB-MATV and early PET response were strongly related to outcome. Baseline WB-MATV and early PET response were both identified by multivariate analyses as independent predictors of OS/PFS along with clinical factors (hazard ratio (HR): 2.51, P < 0.001 and 1.47, P = 0.01 for OS; HR: 1.86, P < 0.001 and 1.84, P < 0.001 for PFS for WB-MATV and early PET response, respectively). Combining WB-MATV (\geq vs. <100 cm³, high vs. low) and early PET response (R vs. NR) allowed identification of four and three distinct subgroup of patients for OS and PFS with significant different median OS (mOS) and PFS (mPFS) (mOS of 13 months for R patients with low-MATV, 8.9 mo for NR/low-MATV, 5.2 mo for R/ high-MATV, and 3.7 mo for NR/ high-MATV; mPFS of 5 mo for R/low-MATV, 3 mo for NR/low-MATV or R/ high-MATV, and 1.3 mo for NR/ high-MATV).

Conclusions : This study confirms the added prognostic value of early PET response on baseline WB-MATV among the commonly used clinical factors for both OS and PFS in chemorefractory mCRC patients treated with multikinase inhibitors. Allowing a more accurate stratification of patients, the combination of these two PET biomarkers should become essential tools to support oncologists in tailoring therapy strategies to the patients' individual risk.

- 002 -

NEUROENDOCRINE NEOPLASMS GRADE 3: PROSPECTIVE OVERALL SURVIVAL DATA AND SURVIVAL AFTER PLATINUM-ETOPOSIDE CHEMOTHERAPY WITHIN AN ENETS CENTER OF EXCELLENCE. A. Cuypers (1), T. Vandamme (1), L. De Backer (2), S. Stroobants (2), M. Simoens (3), I. Dero (4), A. Driessen (2), B. Op De Beeck (2), W. Demey (5), W. Lybaert (6), M. Peeters (2), I. On Behalf Of The Steering Committee and All Net-Specialists (1) / [1] Universiteit Antwerpen / Antwerp University Hospital, WILRIJK (Antwerpen), Belgium, NETwerk,

[2] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, NETwerk, [3] ZNA Jan Palfijn, Merksem, Belgium, NETwerk, [4] Sint Augustinus Ziekenhuis GZA, Antwerp, Belgium, NETwerk, [5] KLINA, Brasschaat, Belgium, NETwerk, [6] AZ Nikolaas, Sint-Niklaas, Belgium, NETwerk.

Introduction : Overall survival (OS) and progression-free survival (PFS) data of grade 3 NENs remains limited.

Aim : The aim is to report prospective survival data in grade 3 NENs treated within NETwerk.

Methods : Patient characteristics of all grade 3 NENs treated from April 2016 to May 2018 were prospectively recorded. Median OS (mOS) from diagnosis and mOS and median PFS (mPFS) after start cisplatinum/carboplatinum-etoposide chemotherapy was calculated.

Results : Of 79 included NEN grade 3 patients, there were 46 males (58,2%). Mean age at diagnosis was 68 years [range 22-90y]. In 67% (N=53) of the cases, the primary tumor was a GEP-NEN (of which 18 unknown). In our population 44% (N=35) had metastases at diagnoses, 44% (N=35) had a Ki67 index $\geq 55\%$, 30% (N=24) had a Ki67 index $< 55\%$. Platinum-etoposide chemotherapy was given in 29% (N=23) of the patients. The majority (N=41) had FDG-PET imaging of which 36 were positive and 14 had somatostatin receptor imaging (SRS) of which 11 were positive. Combined FDG-SRS positivity was seen in 5 of 11 patients (45%). Overall mOS was 10.5m (95%CI: 6.6-NR). In GEP-NEN mOS was 8.3m (95% CI: 6.0-18.7), while in NENs from other origin mOS was 12m (95% CI: 6.8-NR, $p = 0.2$). The mOS for patients with a Ki67 index $< 55\%$ was 14.2m (95% CI: 8.9-NA) vs 8.2m (95% CI: 5.6-NA) for patients with Ki67 index $\geq 55\%$ ($p=0.3$). In multivariate analysis, age at diagnosis had significant impact on OS (HR 0.95, $p=0.003$), while tumor origin showed trend towards significance (HR 0.49, $p= 0.056$). The mPFS and mOS after chemotherapy were 6.5m (95%: 4.8 -NR) and 14.2m (95% CI: 8.3-NR). For the chemotherapy-treated group no significant effect of tumor location, metastasis at diagnosis and age at diagnosis was seen on OS and PFS.

Conclusions : In this grade 3 NEN cohort, non-GEP-NENs have a better OS survival than GEP-NENs. Our results confirm the limited PFS and OS after platinum-etoposide chemotherapy in grade 3 NENs, highlighting the need for better treatment. When performed, FDG-PET and SRS-positivity is frequent and could guide treatment.

- 003 -

TARGETING CD70-POSITIVE CANCER ASSOCIATED FIBROBLASTS TO TACKLE THE IMMUNE SUPPRESSIVE TUMOR MICROENVIRONMENT IN COLORECTAL CANCER. J. Jacobs (1), O. De Wever (2), T. Flieswasser (1), F. Lardon (1), C. Deben (1), V. Siozopoulou (3), H. Prenen (4), M. Peeters (5), E. Smits (1), P. Pauwels (3) / [1] University of Antwerp, Antwerp, Belgium, Center for Oncological Research (CORE), [2] University Hospital Gent, Belgium, Laboratory of Experimental Cancer Research, Department of Radiation Oncology and Experimental Cancer Research, [3] Antwerp University Hospital, Antwerpen, Belgium, Department of Pathology, [4] Antwerp University Hospital, Antwerpen, Belgium, Phase 1-Early Clinical Trials Unit, [5] Antwerp University Hospital, Antwerpen, Belgium, Department of Oncology.

Introduction : Cancer cells are embedded in stroma, the connective tissue framework of solid tumors. In colorectal cancer (CRC), cancer-associated fibroblasts (CAFs) are the main cellular components of the tumor reactive stroma and support tumor progression and invasiveness. However, CAFs represent a heterogeneous population with both cancer-promoting and -restraining actions, lacking specific markers to target them. Expression of immune checkpoint CD70 is normally tightly regulated and limited to cells of the lymphoid lineage. Instead, expression of CD70 on tumor cells has been shown in different malignancies, enabling immune evasion by increasing the amount of suppressive regulatory T cells (Tregs). We have previously revealed the expression of CD70, not on the cancer cells, but highly expressed on a subset of CAFs in invasive CRC specimens. Moreover, CD70-positive CAFs were strongly associated with poor clinicopathological parameters and inferior prognosis.

Aim : In this study, we aimed at investigating the migratory capacities of CD70-positive CAFs and their role in immune escape.

Methods : Primary CAF cell lines were divided into a CD70^{low} and CD70^{high} CAF subpopulation by cell-sorting (FACS Aria II) and used in transwell migration, scratch wound migration (IncuCyte Zoom system) and spheroid migration assays. Co-cultures with CD4⁺ T-cells were set-up to investigate the effect of CD70-positive CAFs on regulatory T-cells by multicolour flow cytometry. Supernatants was collected for cytokine analysis using electrochemiluminescence (MSD). Finally, whole transcriptome-sequencing was performed using the mRNA-Seq Library Prep kit (Lexogen) on CD70^{low} and CD70^{high} CAFs.

Results : CD70^{high} CAFs significantly stimulated migration and increased the production of IL-6. We also revealed a significant increase in the amount of Tregs and production of interleukin-2 upon co-culture of CD4⁺ T-cells with CD70^{high} CAFs, as opposed to CD70^{low} CAFs. Finally, experiments aimed at unravelling the underlying mechanism of CD70-positive CAFs are currently being analysed.

Conclusions : We have identified a targetable CAF subpopulation, marked by the expression of CD70 and equipped with strong migratory capabilities. Thereby, we found evidence of a cross talk between CD70⁺ CAFs and Tregs, paving the way towards immune escape. As such, this study provides a strong rationale for our ongoing exploration of CD70-targeting antibodies in CRC, especially in light of the limited immunotherapeutic options available in CRC.

BASELINE HIGH LEVELS OF CELL-FREE DNA AND THE EARLY INCREASE OF AT LEAST ONE MUTATION ARE INDEPENDENT PROGNOSTIC BIOMARKERS FOR PATIENTS WITH ADVANCED COLORECTAL CANCER UNDER REGORAFENIB. P. Kehagias (1), C. Vandeputte (1), L. Ameye (2), H. El Housni (3), A. Deleporte (1), K. Geboes (4), T. Delaunoy (5), G. Demolin (6), M. Peeters (7), L. D'hondt (8), J. Janssens (9), J. Carrasco (10), S. Holbrechts (11), J. Goeminne (12), P. Vergauwe (13), J. Van Laethem (14), G. Ghanem (15), M. Paesmans (2), P. Flamen (16), A. Hendlisz (1) / [1] Institut Jules Bordet, Brussels, Belgium, Digestive Oncology, [2] Institut Jules Bordet, Brussels, Belgium, Data Centre, [3] Hopital Erasme, ULB, Belgium, Medical Genetics, [4] Universitair ziekenhuis Gent, Belgium, Digestive Oncology, [5] Hôpital de Jolimont, Haine-Saint-Paul, Belgium, Oncology, [6] Centre Hospitalier Chrétien St-Joseph, Liège, Belgium, Gastroenterology, [7] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Oncology, [8] CHU UCL Namur, Site de Godinne, Yvoir, Belgium, Oncology, [9] AZ TURNHOUT, Turnhout, Belgium, Gastroenterology, [10] Grand Hopital de Charleroi, Charleroi, Belgium, Oncology, [11] Centre Hospitalier Universitaire Ambroise Paré Mons, Mons, Belgium, Oncology, [12] Cliniques et Maternité Ste Elisabeth Namur, Namur, Belgium, Oncology, [13] AZ Groeninge, Kortrijk, Belgium, Gastroenterology, [14] Hopital Erasme, ULB, Belgium, Medico-Surgical department of Gastroenterology, [15] Institut Jules Bordet, Brussels, Belgium, Laboratory of Oncology and Experimental Surgery, [16] Institut Jules Bordet, Brussels, Belgium, Nuclear Medicine Imaging and Therapy Department.

Introduction : Circulating cell-free DNA (cfDNA) and the monitoring of tumor-specific mutations are among the hottest topics in solid oncology.

Aim : The combination of baseline (BL) cfDNA levels and circulating tumor DNA (ctDNA) dynamics, based on tumor-specific mutations assessment after 14 days (D14) of therapy, is explored regarding the outcome of patients with advanced colorectal cancer (aCRC) treated with regorafenib.

Methods : Archival tumor tissue and plasma samples at BL and D14 after regorafenib initiation were prospectively collected in aCRC patients (n = 141) in the RegARd-C multicentric trial (NCT01929616). Tumor-specific mutations were selected based on their allelic frequency obtained from a CRC-oriented targeted sequencing of tumor tissue. All available (median 2 (range 1-4)) mutations were monitored for ctDNA assessment at BL and D14 via droplet digital PCR (Bio-Rad QX200 ddPCR system).

Results : The cfDNA's optimal cutoff at BL (Contal & O'Quigley method) is 50 ng/ml of plasma in 134/141 evaluable patients. High BL cfDNA levels (≥ 50 ng/mL), as compare to low levels (< 50 ng/mL), are associated with a worse median PFS (mPFS) (HR 2.50, 95% CI 1.73-3.63, $P < 0.001$) and median OS (mOS) (HR 3.83, 95% CI 2.57-5.71, $P < 0.001$). The most common mutated genes, in 96 evaluable patients for ctDNA assessment, are APC (73%), TP53 (72%), KRAS (66%), and PI3KCA (23%). According to the Contal and O'Quigley's method-defined optimal cut-off of 50%, an increase of at least 1 tumor-specific mutation, as compare to none, between BL and D14 is associated with a worse mPFS of 1.2 vs 3.0 months (HR 2.33, 95% CI 1.51-3.58, $P < 0.001$) and mOS of 3.0 vs 8.5 months (HR 2.33, 95% CI 1.52-3.55, $P < 0.001$) respectively. BL cfDNA level and ctDNA dynamics between BL and D14 are not statistically correlated ($P = 0.23$), and combined, define 4 subgroups with different prognosis.

Conclusions : CfdNA and early ctDNA changes, respectively before and during treatment are independently correlated with the patients' outcome in aCRC treated with regorafenib. Their combined use lays the ground for an enhanced personalization of the patients' management.

STRATIFICATION OF PANCREATIC DUCTAL ADENOCARCINOMAS BASED ON TUMOR AND MICROENVIRONMENT FEATURES. F. Puleo (1), R. Nicolle (2), Y. Blum (2), J. Cros (3), P. Demetter (4), E. Quertinmont (5), M. Svrcek (6), J. Iovanna (7), D. Franchimont (8), L. Verset (4), M. Gomez Galdon (4), J. Devière (8), A. de Reyniès (2), P. Laurent-Puig (9), J. Van Laethem (8), J. Bachet (10), R. Maréchal (8) / [1] Institut Jules Bordet, Brussels, Belgium, Medical Oncology, [2] Programme Cartes d'Identité des Tumeurs (CIT), Ligue Nationale Contre Le Cancer, Paris, France, Programme Carte d'Identité des Tumeurs, [3] Hôpital Beaujon – Hôpitaux Universitaires Paris Nord Val de Seine, Clichy, France, Pathology, [4] Institut Jules Bordet, Brussels, Belgium, Pathology, [5] Erasme Hospital, Brussels, Belgium, Laboratory of Experimental Gastroenterology, [6] Hopital Saint-Antoine, Paris, France, Pathology, [7] University of Marseille, Marseille, France, INSERM, [8] Erasme Hospital, Brussels, Belgium, Gastroenterology and Digestive Oncology, [9] Paris Descartes, CPSC, Paris, France, INSERM, [10] Hôpital Pitié Salpêtrière, Paris, France, Gastroenterology and Digestive Oncology.

Introduction : Genomic studies have revealed subtypes of pancreatic ductal adenocarcinoma (PDA) based on their molecular features, but different studies have reported different classification systems. It is a challenge to obtain high-quality, freshly frozen tissue for clinical analysis and determination of PDA subtypes.

Aim : We aimed to redefine subtypes of PDA using a large number of formalin-fixed and paraffin-embedded PDA samples, which are more amenable to routine clinical evaluation.

Methods : We collected PDA samples from 309 consecutive patients who underwent surgery from September 1996 through December 2010 at 4 academic hospitals in Europe; nontumor tissue samples were not included. Samples were formalin fixed and paraffin embedded. DNA and RNA were isolated; gene expression, targeted DNA sequencing, and immunohistochemical analyses were performed. We used independent component analysis to deconvolute normal, tumor, and microenvironment transcriptome patterns in samples. We devised classification systems from an unsupervised analysis using a consensus clustering approach of our data set after removing normal contamination components. We associated subtypes with overall survival and disease-free survival of patients using Cox proportional hazards regression with estimation of hazard ratios and 95% confidence interval. We used The Cancer Genome Consortium and International Cancer Genome Consortium PDA data sets as validation cohorts.

Results : We validated the previously reported basal-like and classical tumor-specific subtypes of PDAs. We identified features of the PDA, including microenvironment gene expression patterns, that allowed tumors to be categorized into 5 subtypes, called pure basal like, stroma activated, desmoplastic, pure classical, and immune classical. These PDA subtypes have features of cancer cells and immune cells that could be targeted by pharmacologic agents. Tumor subtypes were associated with patient outcomes, based on analysis of our data set and the International Cancer Genome Consortium and The Cancer Genome Consortium PDA data sets. We also observed an exocrine signal associated with acinar cell contamination (from pancreatic tissue).

Conclusions : We identified a classification system based on gene expression analysis of formalin-fixed PDA samples. We identified 5 PDA subtypes, based on features of cancer cells and the tumor microenvironment. This system might be used to select therapies and predict patient outcomes. We found evidence that the previously reported exocrine-like (called ADEX) tumor subtype resulted from contamination with pancreatic acinar cells.

- 006 -

“NEOPAC”: A MULTI-CENTRIC PROSPECTIVE OBSERVATIONAL REGISTRY ON THE NEOADJUVANT THERAPEUTIC APPROACH TO THE LOCALISED PANCREATIC ADENOCARCINOMA, A COLLABORATIVE INTER-UNIVERSITY PROJECT (ULG – FLCD - UCL – ULB). J. Sippet (1), I. Borbath (1), L. Mans (2), R. Maréchal (2), A. Frère (3), C. Rinken (3), B. Delhougne (3), G. Houbiers (4), C. Hubert (5), J. Closset (6), P. Honoré (7), F. Kreutz (8), H. Kalantari (9), J. Van Laethem (2), D. Van Daele (10) / [1] Clin universitaires St-Luc, UCL, Brussels, Belgium, Gastroenterology, [2] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology, [3] CHR La Citadelle, Belgium, Gastroenterology, [4] CHC, Liège, Belgium, Gastroenterology, [5] Clin universitaires St-Luc, UCL, Brussels, Belgium, Digestive surgery, [6] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Digestive surgery, [7] CHU Liege, Liège, Belgium, Digestive surgery, [8] CHC, Liège, Belgium, Oncology, [9] CHR Verviers, Verviers, Belgium, Oncology, [10] CHU Liege, Liège, Belgium, Gastroenterology.

Introduction : The current therapeutic approach of localised pancreatic adenocarcinoma (L-PDAC) is based on the evaluation of the tumour resectability using radiological criteria and reviewed by expert MD board. These criteria lead to the following three situations: - Resectable tumors, resected and followed by adjuvant chemotherapy - Never resectable tumours, that will receive induction chemotherapy eventually followed by radiotherapy, which is not a standard in locally advanced disease. - Borderline resectable that rely on specific vascular involvement criteria and where neoadjuvant therapy is more and more recommended although based on poor evidence. These recommendations remain however based on observational retrospective studies. It is therefore important that, in our practice, we either conduct these approaches as part of controlled studies, or that we record these data on prospective registries, as proposed herein.

Aim : To implement a multi-centric registry of patients with L-PDAC, prospectively enrolled in a common database in order to 1/evaluate the clinical practice of academic and large general hospitals regarding the multimodal management of L-PDAC and 2/ assess the relevant prognostic factors allowing a surgical R0 resection and its prediction to patient's outcome.

Methods : The project at hand is a multi-centric prospective observational study encompassing patients with L-PDAC (resectable, borderline, or not) and being treated in one of the following centres: UCL Saint-Luc (Brussels), ULB Erasme, CHU Ulg, CH Citadelle, CHC Saint Joseph et CHR Verviers. The recorded data are clinical (gender, age, weight, size, ECOG PS, etc.), biological (CA 19.9 level, bilirubin level, etc.), radiological (tumour location, size, staging of vascular involvement, cTNM, metabolic activity) and pathologic findings. For each patient, administered treatments (neoadjuvant chemotherapy, radiotherapy, adjuvant chemotherapy, type of surgery) were recorded, including tumour response and feasibility/tolerability of the whole therapeutic sequence. Follow up at different time points is planned and ongoing.

Results : From March 2017 to November 2018, 42 patients have been enrolled. Baseline characteristics showed a 1:1 gender ratio, a mean age of 64 years (39-89); ECOG at baseline was 0 (39%), 1 (58%) or 2 (2.4%). Mean tumour size was 39 (+/-18) mm and mean CA 19.9 level was 844 (+/-1728) UI/mL. Tumour localization was head in 51.3%, body and tail in 48.7%. Neoadjuvant chemotherapy has been administered to 33 (86%) patients; mainly Folfirinox (73,7%) or gemcitabine-abraxane (12,3%). Amongst patients that achieved neoadjuvant chemotherapy (25 patients, with a median

number of cycles 5.64), we observed 2 complete response (CR), 12 partial response (PR), 6 stable disease (SD) and only 3 progressive disease (2 patients were not evaluable). Nine patients received neoadjuvant chemo-radiotherapy after chemotherapy. Surgical resection could be performed to 11 patients. Amongst readily resectable patients, 4 out of 5 could undergo surgery. For borderline resectable and locally advanced patients that achieved neo-adjuvant therapy, 7 out of 25 underwent surgery. R0 resection rate was 72.7% (n=8/11), one patient had R1 (after Folfirinox and radiochemotherapy), one patient had R2 (after Folfirinox) and one had Rx (resected at baseline) surgery. Amongst all resected patients, 26.3% are alive without recurrence, 31.6% had a relapse (mainly metastasis), 31.6% are dead (cancer-related in each case) and 10.5% were lost to follow-up.

Conclusions : These preliminary data show Folfirinox to be the main neoadjuvant chosen treatment for borderline resectable and locally advanced L-PDAC. Full neoadjuvant sequence is feasible in most of our patients before attempt of surgery. Enrolment of patients is ongoing in this first multicentric initiative for completing data on perioperative period and outcome. Data on more patients, with more follow-up will be shown at the meeting.

- O07 -

REGORAFENIB AFTER FAILURE OF GEMCITABINE AND PLATINUM-BASED CHEMOTHERAPY FOR LOCALLY ADVANCED (NON RESECTABLE) AND METASTATIC BILIARY TUMORS: A RANDOMIZED DOUBLE-BLINDED PLACEBO-CONTROLLED PHASE II TRIAL. A. Demols (1), I. Borbath (2), M. Van Den Eynde (2), G. Houbiers (3), M. Peeters (4), R. Maréchal (5), T. Delaunoy (6), J. Goeminne (7), S. Laurent (8), S. Holbrechts (9), M. Paesmans (10), J. Van Laethem (1) / [1] Hopital Erasme, ULB, , Belgium, Gastroenterology, [2] Clin universitaires St-Luc, UCL, Brussels, Belgium, Gastroenterology, [3] CHC, Liège, Belgium, Gastroenterology, [4] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Oncology, [5] CHU Tivoli, La Louvière, Belgium, Gastroenterology, [6] Hôpital de Jolimont, Haine-Saint-Paul, Belgium, Gastroenterology, [7] Clinique Sainte-Elisabeth, Namur, Belgium, Oncology, [8] UZGent, Gent, Belgium, Gastroenterology, [9] CHU Ambroise Paré MONS, Mons, Belgium, Oncology, [10] Institut Jules Bordet, Brussels, Belgium, Data center.

Introduction : A high clinical unmet need remains in treating advanced or metastatic biliary tract cancers (BTC) after failure of gemcitabine and platinum-based chemotherapy, with no standard of care. Regorafenib is potent oral multi-kinase inhibitor of kinases involved in tumor angiogenesis, oncogenesis and tumor microenvironment. It has demonstrated efficacy and acceptable safety in some GI tumors that have progressed on standard therapies.

Aim : REACHIN (NCT02162914) is a multicenter double-blinded placebo-controlled randomized phase II study to evaluate the safety and efficacy of regorafenib (REG) in patients with locally advanced (non resectable) and metastatic histologically proven BTC, progressing after gemcitabine-platinum. Primary endpoint is PFS. Secondary endpoints are response rate and OS.

Methods : 66 patients were randomized (1:1) to receive BSC plus REG160 mg od, 3 weeks on/ one week off (cycle= 4 weeks) or BSC + placebo (P) until progression or unacceptable toxicity. Sample size calculation was based on the logrank test, assuming a one-sided significance of 10%, 80% power, and an improvement in median PFS of 50% (6 to 12 weeks in the REG group).

Results : Between May 2014 and February 2018, 68 (33 REG, 35 P) patients have been included (2 patients died before starting treatment and were replaced). Of 66 patients treated (26 F/ 40 M), tumors were intra-hepatic and hilar (n=48), extra-hepatic (n=10) and gallbladder (n=8). One patient remains on REG treatment. Median PFS for REG is 3.0 months (95% CI: 2.3-4.9) and 1.5 months (95% CI : 1.2-2.0) for P with a HR of 0.48 (95% CI : 0.29-0.80), p=0.004. Rates of PR+SD are 23/33 (70%) for REG and 11/33 (33%) for P (p=0,002). Median treatment duration is 10,9 weeks for REG vs 6,3 weeks for P (p=0,004). Dose reductions were applied in 14/33 patients in REG and in 5/33 patients in P. There is no unexpected/new safety signal. Median OS is 5.3 months for REG and 5.1 months for P (p=0.21).

Conclusions : Regorafenib significantly increases median PFS and tumor control in patients with previously treated metastatic/ unresectable biliary tract cancer.

- O08 -

PREOPERATIVE RADIATION THERAPY WITH A SIMULTANEOUS INTEGRATED BOOST COMPARED TO CHEMORADIO THERAPY FOR CT3-4 RECTAL CANCER: A MULTICENTRIC RANDOMIZED STUDY. M. De Ridder (1), A. De Paoli (2), E. Delmastro (3), F. Munoz (4), S. Vagge (5), D. Norkus (6), H. Everaert (7), G. Tabaro (8), E. Garibaldi (3), U. Ricardi (4), E. Borsatti (9), P. Gabriele (3), G. Boz (8), E. Dubaere (10), M. Mahe (11), T. Gevaert (10), B. Engels (10) / [1] UZBrussel, Brussel, Belgium, Radiotherapy, [2] National Cancer Institute, Aviano, Italy, National Cancer Institute, [3] IRCC Candiolo, Candiolo, Italy, IRCC, [4] University of Torino, Torino, Italy, Department of oncology, [5] National Cancer Research Institute and University Of Genoa, Genoa, Italy, IRCCS San Marino IST, [6] National Cancer Institute, Vilnius, Lithuania, National Cancer Institute, [7] UZBrussel, Brussel, Belgium, Department of Nuclear Medicine, [8] National Cancer Institute, Aviano, Italy, National Cancer institute, [9] National Cancer Institute,

Aviano, Italy, National Cancer Institute, [10] UZBrussel, Brussel, Belgium, Radiotherapy, [11] Centre Rene Gauducheau, St. Heblain, France, Centre Rene Gauducheau.

Introduction : Preoperative chemoradiotherapy (CRT) has been established as the standard treatment for T3-4 rectal cancer. As an alternative strategy, we reported previously in a phase II study limited toxicity and high local control (LC) using image-guided and intensity-modulated RT (IG-IMRT) with a simultaneous integrated boost (RTSIB) instead of concomitant chemotherapy.

Aim : The present multicentric randomized trial (NCT01224392) compared this strategy to CRT. Early and late outcome are reported.

Methods : cT3-4 rectal cancer patients were randomly assigned to receive either preoperative IG-IMRT 46Gy/23 fractions plus capecitabine 825 mg/m² twice daily (CRT-arm) or IG-IMRT 46Gy/23 fractions with a SIB to the rectal tumor up to a total dose of 55.2 Gy (RTSIB-arm). Surgery was performed 6-8 weeks after completion of preoperative treatment. Adjuvant chemotherapy consisted in both arms of 6 cycles capecitabine 1000mg/m² twice daily on day 1 to 14, every 3 weeks. Metabolic tumor activity reduction, by measuring the percentage of SUVmax difference on sequential FDG-PET imaging, was the primary short-term endpoint.

Results : A total of 174 patients were randomly assigned to the CRT-arm (n=89) or RTSIB-arm (n=85) between April 2010 and May 2014. Grade 3 acute toxicity was 6% and 4% in the CRT- and RTSIB-arm, respectively. The mean fractional change in SUVmax at 5 weeks after completion of preoperative RT was -55.8% (\pm 24.0%) and -52.9% (\pm 21.6%) for patients in the CRT-arm and RTSIB arm, respectively (p=0.43). There were no significant differences in sphincter preservation (75% vs 68%) and R0 resection rate (98% vs 97%). The pathologic complete response rate (pCR) rate was 24% with CRT compared to 14% with RTSIB (p=0.13). Dworak grade 3-4 rates were comparable between both arms (49% for CRT vs 45% in the RTSIB-arm). Adherence to a full course of adjuvant chemotherapy was low (34% in the CRT-arm and 31% in the RTSIB-arm). After a median follow-up of 48 months, we report a 5-year overall survival (OS) of 76.1% in the CRT-arm vs 74.8% for the RTSIB-arm (p=0.91). There were no differences between treatment arms either for 5-year progression-free survival (PFS) (54.7% for CRT vs 55.4% for RTSIB, p=0.48) and 5-year LC (94.3% for CRT and 93.4% for RTSIB, p=0.42). The absolute incidence of any grade \geq 3 late gastrointestinal and urinary toxicity was 7% and 5% for CRT whereas 5% and 4% for RTSIB patients, respectively.

Conclusions : The preoperative RTSIB approach was not inferior to CRT in terms of OS, PFS and LC in the current study. Acute and late toxicity did not differ between treatment arms. RTSIB represents a promising alternative to CRT in patients with cardiac comorbidity or other contra-indications for 5-fluorouracil based chemotherapy.

- 009 -

COMBINED GA-DOTATATE AND FDG PET/CT IMAGING IMPROVES PROGNOSTIC STRATIFICATION IN METASTATIC GASTROENTEROPANCREATIC NEUROENDOCRINE NEOPLASIAS. I. Karfis (1), H. Levillain (2), G. Marin (2), G. Critchi (2), L. Taraji Schiltz (2), R. Muteganya (2), L. Shaza (3), L. Mans (3), M. Elbachiri (3), A. De Matos Pereira (2), Z. Wimana (2), G. Machiels (3), A. Hendlisz (3), P. Flamen (2) / [1] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, Nuclear Medicine, [2] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, Nuclear Medicine, [3] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, Digestive Oncology.

Introduction : Histological tumor grading (based on the Ki67 proliferation index) is a validated prognostic biomarker in gastroenteropancreatic neuroendocrine neoplasias (GEP-NENs), widely used in clinical practice. Molecular Imaging techniques such as Ga-DOTATATE and FDG PET/CT may provide additional prognostic information over Ki67 in terms of biological behaviour.

Aim : The study aimed to assess the added prognostic value of combined, integrated, Ga-DOTATATE/FDG PET/CT molecular imaging compared to Ki67-based histological grading in patients with metastatic GEP-NENs.

Methods : 87 consecutive patients with histologically proven metastatic GEP-NENs who underwent combined PET/CT imaging from 01/2004 to 12/2017 were retrospectively evaluated. Highest Ki67 value (ENETS 2017 classification) available at time of FDG PET/CT was recorded (median time between Ki67 date and FDG PET/CT date: 18.8 months, range: 0.1-126.4 months). Patients were stratified according to ENETS histological grades (G1, G2 and G3) and in three distinct imaging categories (C1: all lesions Ga-DOTATATE+/FDG-, C2: at least one Ga-DOTATATE+/FDG+ lesion and C3: at least one Ga-DOTATATE-/FDG+ lesion). The primary endpoint of the study was Progression-Free Survival, assessed from the date of FDG PET/CT to the date of radiological disease progression.

Results : Stratification according to ENETS grade did not show significant statistical difference in median PFS (mPFS) between G1 and G2 patients [14.9 vs 24.1 months, p=0.58]. mPFS was significant between G2 and G3 patients [24.1 vs 6.1 months, p<0.001]. In contrast, mPFS was significantly higher in C1 patients compared to C2 [24.0 vs 15.2 months, p=0.031] and in C2 compared to C3 [15.2 vs 4.7 months, p=0.002] patients.

Conclusions : Combined Ga-DOTATATE/FDG PET/CT imaging significantly improves prognostic stratification in patients with metastatic GEP-NENs. These data suggest that imaging, as whole-body molecular and metabolic mapping procedure, should precede and guide (re)-biopsy towards the most aggressive/FDG avid part of the disease, if any.

EFFICACY, SAFETY, AND PATIENT-REPORTED OUTCOMES IN PATIENTS WITH HEPATOCELLULAR CARCINOMA WITH ALPHA-FETOPROTEIN ≥ 400 NG/ML: A POOLED ANALYSIS FROM REACH AND REACH-2 STUDIES. I. Borbath (1), M. Kudo (2), R. Finn (3), P. Galle (4), J. Llovet (5), J. Blanc (6), T. Okusaka (7), I. Chau (8), D. Cella (9), M. Peck-Radosavljevic (10), A. Girvan (11), J. Gable (11), L. Bowman (11), P. Abada (12), Y. Hsu (13), A. Zhu (14) / [1] Université Catholique de Louvain, Brussels, Belgium, HepatoGastroenterology and Digestive Oncology, [2] Kindai University Faculty of Medicine, Osaka, Japan, Department of Gastroenterology and Hepatology, [3] Los Angeles Medical Center, University of California, Los Angeles, United States (the), Department of Medicine, [4] Universitätsmedizin Mainz, Mainz, Germany, First Department of Internal Medicine, [5] Mount Sinai School of Medicine, New York, United States (the), Department of Medicine, [6] CHU Bordeaux Hopital St. André, Bordeaux, France, Department of Hepato-gastroenterology and Medical Oncology, [7] National Cancer Center Hospital, Tokyo, Japan, Department of Hepatobiliary and Pancreatic Oncology, [8] The Institute of Cancer Research/Royal Marsden NHS Foundation Trust, Sutton, United Kingdom (the), Department of Medicine, [9] Northwestern University, IL, United States (the), Department of Medical Social Sciences, [10] Klinikum Klagenfurt am Wörthersee, Klagenfurt am Wörthersee, Austria, Department of Internal Medicine & Gastroenterology, [11] Eli Lilly and Company, Belgium, Global Patient Outcomes and Real World Evidence, [12] Eli Lilly and Company, Belgium, Medical Affairs, [13] Eli Lilly and Company, Belgium, Statistics-Oncology, [14] Massachusetts General Hospital, Boston, United States (the), Department of Hematology/Oncology.

Introduction : Hepatocellular carcinoma (HCC) is one of the leading causes of cancer-related death. The advanced disease is associated with worsening of quality of life in patients with HCC. Ramucirumab (RAM) has shown survival benefits in patients with alpha-fetoprotein (AFP) ≥ 400 ng/ml who failed prior sorafenib treatment.

Aim : Here, we present efficacy, safety, and patient-reported outcomes in patients with HCC and AFP ≥ 400 ng/ml

Methods : This is a meta-analysis of individual patient level data from two phase 3, randomized, placebo-controlled: REACH and REACH-2 studies. Eligibility criteria were the same in both studies (except for AFP levels ≥ 400 ng/ml in REACH-2): prior sorafenib, advanced HCC (BCLC-C), Child- Pugh score < 7 , ECOG PS 0 or 1. Patients received RAM (8mg/kg) or placebo (PBO) on day 1 every 14 days. Patient-reported outcomes were assessed using Functional Assessment of Cancer Therapy (FACT) Hepatobiliary System Index (FHSI)-8 (score decrease of ≥ 3 was defined as deterioration). Time to deterioration (TTD) was time from the date of randomization to the date of first deterioration in FHSI-8. Efficacy assessment included overall survival (OS), progression-free survival (PFS), objective response rate (ORR), and safety.

Results : Overall, 542 patients were pooled from REACH with AFP ≥ 400 ng/ml (n=250) and REACH-2 (n=292); 316 patients were in RAM and 226 in PBO group. Improved OS (RAM, 8.1 mo vs PBO, 5.0 mo; HR 0.694; 95% CI 0.571-0.842; $p < .0002$) and prolonged PFS (RAM, 2.8 mo vs PBO, 1.5 mo; HR 0.572, 95% CI 0.472-0.694; $p < .0001$) were reported in patients treated with RAM vs PBO. ORR was also improved (5.4% RAM vs 0.9% PBO [$p < .004$]). TTD of the FHSI-8 total score was significantly delayed in patients treated with RAM compared to PBO (3.3 months in RAM group vs 1.9 months in PBO; HR 0.725, 95% CI 0.559-0.941). Overall, 9.5% and 3.6% of patients discontinued due to adverse events (AEs) in RAM and PBO group, respectively. Hypertension (12.0% RAM vs 3.6% PBO) and hyponatremia (5.1% RAM vs 2.2% PBO) were the only grade ≥ 3 treatment-emergent adverse events occurring in $\geq 5\%$ in RAM.

Conclusions : RAM significantly improved OS, PFS, ORR, and delayed deterioration of PROs in HCC patients with AFP > 400 ng/mL with an acceptable safety profile.

FAT QUALITY: THE HANDSOME STRANGER IN ESOPHAGEAL CANCER PROGNOSIS. M. Anciaux (1), L. Ameye (2), T. Guiot (3), P. Flamen (3), S. Goldman (4), P. Demetter (5), A. Deleporte (6), M. Paesmans (7), V. Donckier (8), A. Van Gossum (9), A. Hendlisz (6), C. Vandeputte (1) / [1] Institut Jules Bordet, Brussels, Belgium, Digestive Oncology Laboratory, [2] Institut Jules Bordet, Brussels, Belgium, Data Centre, [3] Institut Jules Bordet, Brussels, Belgium, Department of Nuclear Medicine, [4] Erasme Hospital, Brussels, Belgium, Department of Nuclear Medicine, [5] Institut Jules Bordet, Brussels, Belgium, Department of Pathology, [6] Institut Jules Bordet, Brussels, Belgium, Medical Oncology Department, [7] Institut Jules Bordet, Brussels, Belgium, Data centre, [8] Institut Jules Bordet, Brussels, Belgium, Department of Surgery, [9] Erasme Hospital, Brussels, Belgium, Medico-Surgical Department of Gastroenterology.

Introduction : Esophageal cancer (EC) is an aggressive cancer with an increasing worldwide incidence, particularly for adenocarcinoma (ADC). ADC develops over chronic gastroesophageal reflux disease (GERD), which has been associated with obesity. Moreover, esophageal patients often present an important weight loss at diagnosis, due to dysphagia. The loss of skeletal muscle, also called sarcopenia, has been associated with poor survival in multiple cancers. Conversely, the role of adipose tissue is not well studied.

Aim : We aimed to assess the association of several criteria of cachexia at diagnosis, namely body-mass index (BMI), weight loss, inflammation, muscle mass and adipose tissue, with Overall Survival (OS) in a large retrospective cohort of EC patients.

Methods : Diagnostic CT scans were assessed for BMC in 155 all-stages EC patients at diagnosis. The index (area/height²) of skeletal muscle (SMI), subcutaneous (SFI) and visceral fat (VFI) were delineated on two adjacent slides at the third lumbar vertebra level by two independent investigators using PLANET ONCO® software (DOSIsoft, France). Mean attenuation (or density) of fat tissue was measuring to assess the quality of adipose compartments. Survival and relapse free survival (RFS) were calculated from date of baseline CT-scan.

Results : Interobserver correlation was excellent for all BMC parameters measured ($r = 0.94$ to 0.99). Remarkably, low subcutaneous fat density (SFD) was associated to better outcome (HR = 2,2, 95% CI =1,4-3,5 , P =0,0003), as was low disease stages (HR=2,2, 95% CI =1,2-3,7, P =0,0047). Low C-reactive protein (CRP) levels were associated with better overall survival (OS) (HR=2,2, 95% CI = 1,2-3,8, P = 0,0053). In contrast, low BMI did not distinguish patients' outcome (HR=0,71, 95% CI = 0,46-1,1, P = 0,13). Relapse free survival (RFS) analysis showed that only low disease stages (HR = 1,8, 95% CI = 1-3,1, P = 0,044) and low SFD (HR = 1,6, 95% CI = 1-2,6, P = 0,04) remained associated to improved RFS. Stepwise regression showed that the combination of SFD, stages and CRP was an effective model for OS prediction. No parameter was retained for RFS in stepwise regression model.

Conclusions : SFD, stages and CRP appeared as robust prognostic factors in EC patients, in contrast with BMI. The multivariate analysis showed that the combination of these factors, or each individual factor, composed effective models for OS prediction in EC. While SFD and stages were significant in RFS univariate analysis, none of these two parameters were retained in multivariate analyses. These results confirm the validity of body-mass composition assessment for evaluating patient prognosis. This study questions the fundamental mechanism of density variation in adipose tissue, in EC but also in other cancers. This subject should be properly further investigated.

- O12 -

IS A SINGLE DRIVER GENE MUTATION SUFFICIENT FOR MONITORING EARLY RESPONSE IN ADVANCED COLORECTAL CANCER? P. Kehagias (1), C. Vandeputte (1), L. Ameye (2), H. El Housni (3), A. Deleporte (1), K. Geboes (4), T. Delaunoy (5), G. Demolin (6), M. Peeters (7), L. D'hondt (8), J. Janssens (9), J. Carrasco (10), M. Gomez Galdon (11), P. Heimann (3), M. Paesmans (2), P. Flamen (12), A. Hendlisz (1) / [1] Institut Jules Bordet, Brussels, Belgium, Digestive Oncology, [2] Institut Jules Bordet, Brussels, Belgium, Data Centre, [3] Hopital Erasme, ULB, Belgium, Medical Genetics, [4] Universitair ziekenhuis Gent, , Belgium, Digestive Oncology, [5] Hôpital de Jolimont, Haine-Saint-Paul, Belgium, Oncology, [6] Centre Hospitalier Chrétien St-Joseph, Liège, Belgium, Gastroenterology, [7] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Oncology, [8] CHU UCL Namur, Site de Godinne, Yvoir, Belgium, Oncology, [9] AZ TURNHOUT, Turnhout, Belgium, Gastroenterology, [10] Grand Hopital de Charleroi, Charleroi, Belgium, Oncology, [11] Institut Jules Bordet, Brussels, Belgium, Pathology, [12] Institut Jules Bordet, Brussels, Belgium, Nuclear Medicine Imaging and Therapy Department.

Introduction : Circulating tumor DNA (ctDNA) monitoring based on an individual mutation profile during therapy is under intense investigation in modern oncology. We previously reported that the increase of $\geq 50\%$ of at least one somatic mutation among multiple monitored mutations per patient is associated with a significantly worse outcome (P. Kehagias, et al., AACR; Cancer Res 2018;78(13 Suppl)).

Aim : This study investigates whether the ctDNA monitoring of one driver gene mutation, provides enough information as compared to multiple mutations to assess response to regorafenib in advanced chemorefractory colorectal cancer (aCRC) at an early timepoint.

Methods : Archival tumor tissue and plasma samples (PL) at baseline (BL) and 14 days (D14) after treatment initiation in aCRC pts (n=141) were prospectively collected in the RegARd-C multicenter clinical trial (NCT01929616). Somatic mutations were identified based on a CRC-oriented targeted gene sequencing of tumor tissue. All available (median 2 (1-4)) driver gene mutations were monitored per patient in PL at BL and D14 via droplet digital PCR (Bio-Rad QX200 ddPCR system) to assess ctDNA dynamics.

Results : In 96 evaluable patients, the most frequently monitored mutated genes were APC (73%), TP53 (72%), KRAS (66%), and PI3KCA (23%). Among patients with ≥ 2 monitored mutations (73/96), one was selected at random and compared to previous methodology taking in account dynamics of all followed mutations. Optimal cutoff (CO) evaluation (Contal & O'Quigley method) separated patients (n=96) according to a ctDNA increase of $\geq 50\%$ versus an increase of $< 50\%$ or a decrease. The concordance of ctDNA dynamics based on one randomly selected mutation and multiple monitored mutations was 91%. Our data demonstrated that a ctDNA increase based on one single mutation taken at random is significantly associated with a worse clinical outcome in terms of progression-free survival (HR 2.42, 95% CI (1.56-3.74), P<0.001) and overall-survival (HR 2.17, 95% CI (1.41-3.34), P<0.001). In addition, when combining patients' ctDNA dynamics to BL ctDNA levels (\geq or < 5 ng/mL optimal CO) or BL cell-free DNA (cfDNA) levels (\geq or < 50 ng/mL optimal CO), we could distinguish 4 patients' subgroups with different prognosis. However, when performing a multivariate analysis including clinical parameters, BL ctDNA and BL cfDNA levels, BL ctDNA was not relevant in the presence of BL cfDNA.

Conclusions : The monitoring of ctDNA dynamics based on only one randomly selected driver gene mutation versus multiple is equally informative to describe adequately aCRC patients' outcome under regorafenib after 14 days of treatment onset. Especially, combined with pre-treatment ctDNA levels, this simplifies a personalized patient monitoring.

- O13 -

THE PROGNOSTIC VALUE OF KRAS, NRAS, BRAF AND DNA MISMATCH REPAIR (MMR) STATUS IN LEFT- AND RIGHT-SIDED METASTATIC COLORECTAL CANCER (mCRC): A BELGIAN POPULATION-BASED STUDY. K. Janssens (1), G. Van Camp (2), K. Op De Beeck (2), E. Fransen (3), N. Van Damme (4), M. Peeters (5) / [1] University of Antwerp, Antwerp, Belgium, Internal medicine, [2] Center of Oncological Research (CORE), Wilrijk, Belgium, Center of Oncological Research, [3] University of Antwerp, Antwerp, Belgium, StatUa Center for Statistics, [4] Stichting Kankerregister, Brussel, Belgium, Belgian Cancer Registry, [5] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Department of Oncology.

Introduction : In recent years, the difference in survival between right-sided and left-sided colorectal cancer (CRC) has been extensively studied. Various studies have convincingly shown that patients with tumors originating on the left side of the colon have a significantly better prognosis than those with tumors originating on the right side of the colon, in all CRC stages. However, the underlying mechanisms that cause this difference in survival have not been identified yet. It has been hypothesized that KRAS, NRAS or BRAF mutations and microsatellite instability (MSI) are (at least partially) responsible for the prognostic effect of primary tumor location.

Aim : The aim of this study is to evaluate the prognostic effect of tumor primary location combined with DNA MMR status and BRAF and RAS mutational status in the (non-selected) Belgian population.

Methods : In Belgium, data on patient and tumor characteristics of all new diagnosed cancers is collected in a national and population based cancer registry, the Belgian Cancer Registry (BCR). A random sample of 1,035 patients diagnosed with de novo stage IV CRC in 2014 was included in our analysis. We obtained information on age, sex, stage, location of the primary tumor, biomarker status (RAS, BRAF mutational status and mismatch repair status) and vital status. In order to obtain more data about MMR, we included an additional 1,182 patients diagnosed with mCRC in 2015. The vital status was retrieved by the BCR from the Crossroads Bank of Social Security. Cancers were classified as right-sided cancer if they were located in the caecum, ascending colon, hepatic flexure and transverse colon. Left-sided colon cancer was defined as cancer of the splenic flexure, descending colon, sigmoid and rectosigmoid colon.

Results : We included 1,035 mCRC patients diagnosed in 2014. We excluded 177 patients with a second tumor and 26 patients with tumors located in the appendix or with overlapping or unspecified tumor location. The final study population consisted of 832 mCRC patients; 268 (32.2%) located at the right side of the colon, 352 (42.3%) located at the left side of the colon and 212 (25.5%) rectal cancers. We included another 1182 metastatic colorectal cancer patients diagnosed in 2015, in order to collect a sufficient amount of data to analyze DNA MMR status. In this subgroup of 1182 mCRC, we excluded 171 patients with a second tumor and 25 patients with tumors located in the appendix or with overlapping or unspecified tumor location. KRAS and NRAS mutational status did not have a significant prognostic value in our study population and did not modify the prognostic effect of primary tumor location. BRAF mutational status had a significant impact on survival ($p = 0.00107$), but did not modify the prognostic effect of primary tumor location. We observed a significant increase in hazard for patients with a BRAF mutation. For MSI, we found a strong association between location and MMR ($p=4.4E-6$), with the abnormal MMR being more frequent among the right-sided cancer patients. Due to this multicollinearity, the main effect of MMR is not significant in a Cox Proportional Hazard model that includes location as covariate. Across all models, mean survival time was shorter in the right-sided tumors.

Conclusions : We studied the survival rates in patients diagnosed with mCRC in 2014. Currently, we can conclude that in mCRC left-sided tumors have a better prognosis than right-sided tumors, regardless of RAS and BRAF mutational status or microsatellite instability. This corresponds with findings of previous research. Further research should focus on identifying the underlying complex molecular mechanisms that cause this difference in survival between left-sided and right-sided mCRC.

- O14 -

INDEPENDENT COHORT VALIDATION OF THE NEGATIVE PROGNOSTIC IMPACT OF HIGH VISCERAL ADIPOSE TISSUE DENSITY IN ADVANCED COLORECTAL CANCER. C. Vandeputte (1), A. Deleporte (1), T. Guiot (2), L. Ameye (3), M. Paesmans (3), P. Flamen (2), A. Hendlisz (4) / [1] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, medical oncology, [2] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, Department of Nuclear Medicine, [3] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, Information management unit, [4] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, Medical oncology.

Introduction : While obesity is a risk factor for the development of colorectal cancer (CRC), it could be associated with prolonged overall survival after (OS) cancer diagnosis. Loss of skeletal muscle, or sarcopenia, has also been associated

with poor survival in multiple cancers including CRC. Conversely, the role of adipose tissue is not well studied. Our group has recently shown the negative prognostic impact of low muscle index and muscle density as well as high visceral adipose tissue density on survival in metastatic CRC patients included in the clinical studies SoMore (NCT01290926) and RegARd-C (NCT01929616). We also demonstrated a protective role of obesity in CRC patients at an advanced stage.

Aim : To validate these results in an independent cohort of advanced CRC patients.

Methods : External validation of previous findings was performed in 47 among 55 advanced CRC patients included in the clinical trial CORIOLAN (NCT01591590). The primary objective of CORIOLAN is to investigate if the spontaneous evolution of the tumoral metabolic progression index by serial FDG PET-CT is related to the patient's outcome. On baseline computed tomography images, muscle, visceral fat and subcutaneous fat were delineated on two adjacent slides at the third lumbar vertebra level using the PLANET Onco® software. The relationship between body composition, BMI and OS was evaluated based on the optimal cutoffs calculated in the SoMore and RegARd-C cohorts and using the appropriate statistics in R.

Results : Patients with a high BMI did not show a significantly better OS (≥ 30 versus < 30). In addition, patients with low muscle index density had no increased mortality. In contrast, low subcutaneous fat index was associated with an increased risk of dying (HR: 1.87; 0.94 – 3.7). Finally, a high subcutaneous and visceral adipose tissue density were correlated with mortality (HR: 2.13; 1.15 – 3.93) and (HR: 2.25; 1.15 – 4.37).

Conclusions : Although our results did not confirm the protective role of obesity and skeletal muscle tissue in advanced CRC, the important prognostic role of visceral adipose tissue density was maintained. Whether the prognostic impact of adipose tissue density in our study is mediated by inflammation and/or malnutrition remains to be investigated.

- O15 -

RESULTS FROM THE OBSERVATIONAL COLONG STUDY OF PATIENTS WITH METASTATIC COLORECTAL CANCER (mCRC) TREATED WITH REGORAFENIB FOR 4 MONTHS OR MORE IN BELGIUM. M. Peeters (1), A. Demols (2), K. Geboes (3), K. Hendrickx (4), D. Van Daele (5), M. Van Den Eynde (6), J. Wilputte (7) / [1] Antwerp University Hospital, Edegem, Belgium, Oncology, [2] Erasme Hospital, Brussels, Belgium, Gastroenterology, [3] UZGent, Gent, Belgium, Gastroenterology, [4] OLV Aalst, Aalst, Belgium, Gastroenterology, [5] CHU Liege, Liège, Belgium, Gastroenterology, [6] Saint-Luc University Hospital, Brussel, Belgium, Oncology, [7] Cliniques Sud Luxembourg, Arlon, Belgium, Gastroenterology.

Introduction : Regorafenib (Stivarga®) improved overall survival versus placebo in the phase 3 CORRECT and CONCUR trials and is approved for the treatment of refractory mCRC. However, there are no data on patients with mCRC treated with regorafenib in a real-world clinical practice setting in Belgium.

Aim : To evaluate long-term responders versus short-term responders

Methods : COLONG is an observational, retrospective, chart review study of patients with mCRC who started treatment with regorafenib between 1 July 2015 and 31 July 2017 in different centers across Belgium. The objective was to examine differences in patients who had a duration of treatment (DoT) with regorafenib ≥ 4 months relative to those with a DoT < 4 months. Descriptive statistics are reported.

Results : Of the 161 patients enrolled in 7 centers, 43 (27%) had a DoT ≥ 4 months (Table) and most of these patients (38/43) were treated for < 12 months; of the 5 patients with a DoT ≥ 12 months, 4 remained on treatment at the time of this analysis. Patients with a DoT ≥ 4 months generally had comparable baseline characteristics to those with a shorter DoT, except that the DoT ≥ 4 subgroup tended to have a higher percentage of patients with ECOG PS 0 and a higher percentage with multiple metastases compared with patients with a DoT < 4 months. KRAS mutation rates were similar. Most patients discontinued treatment due to disease progression (DoT ≥ 4 vs < 4 months: 79% vs 63%). A higher proportion in the DoT ≥ 4 months subgroup received post-regorafenib treatment for mCRC with chemotherapy (IV or oral) and/or biologic therapy (44% vs 34%).

Conclusions : In this retrospective chart review of patients with mCRC treated with regorafenib in Belgium, patients with a DoT ≥ 4 months tended to have a better performance status at baseline.

- O16 -

PERSONALISED SELECTIVE INTERNAL RADIATION THERAPY IMPROVES OUTCOMES IN REFRACTORY INTRA-HEPATIC CHOLANGIOCARCINOMA: A MULTICENTER STUDY. H. Levillain (1), I. Duran Derijckere (1), L. Ameye (2), T. Guiot (3), A. Braat (4), B. Vanderlinden (3), N. Reynaert (3), A. Hendlisz (5), M. Lam (4), C. Deroose (6), H. Ahmadzadehfar (7), P. Flamen (1) / [1] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, Nuclear Medicine, [2] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, Data Center, [3] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, Medical Physics, [4] University Medical Center Utrecht, The Netherlands, Radiology and Nuclear Medicine, [5] Institut Jules Bordet -

Université Libre de Bruxelles (ULB), Brussels, Belgium, GastroIntestinal Unit Medical Oncology Clinic, [6] University Hospitals Leuven, Belgium, Nuclear Medicine, [7] University Hospital Bonn, Bonn, Germany, Nuclear Medicine.

Introduction : An important proportion of patients presenting an intra-hepatic Cholangiocarcinoma (IH-CCA) will relapse post-surgery and/or post-chemotherapy. For this subset of refractory patients selective internal radiation therapy (SIRT) has emerged as an effective treatment modality with median survivals ranging from 7 to 22 months. However, contrasting results after SIRT enlightens the lack of prognostic and predictive biomarkers for patient stratification and treatment optimisation.

Aim : To assess the prognostic value of pretherapeutic clinical, biological and imaging biomarkers extracted from unresectable and refractory IH-CCA patients treated with SIRT and to determine the added value of using a more personalized model: partition-model (PM), for the calculation of the individual activity of ⁹⁰Y-microspheres, compared to the utilization of the standard Body-Surface-Area (BSA) method.

Methods : This retrospective multicentre study enrolled 58 patients with unresectable intrahepatic cholangiocarcinoma (IH-CCA), refractory to surgery and/or chemotherapy, treated with resin ⁹⁰Y-microsphere, in 4 European SIRT expert centres. Clinicopathologic data were collected from patient's records. Metabolic parameters as well as presence of hypermetabolic lymph nodes were measured at baseline FDG-PET/CT. Lesion volume delineation was performed on baseline FDG-PET/CT and then projected on the anatomically registered ^{99m}Tc-MAA-SPECT/CT. MAA lesion uptake to non-tumoural-liver uptake ratio (TLRMAA) was computed for each lesion as well as their mean absorbed dose (Dmean). Univariate associations between variables and OS were examined by the log rank test. Continuous variables were dichotomized by using their respective median as cut-off value. Multivariate Cox's proportional hazards model was then performed to determine the independent prognostic significance of each parameter. Finally, differences between patients treated by BSA and patients treated with PM were investigated using appropriate statistics.

Results : The median OS post-SIRT of the entire cohort was 10.3 months. One-year and the 2-years survival rates were 39.8% and 21.6%. Biological parameters associated with significant differences in terms of OS were albumin (hazard-ratio (HR)=2.78, p=0.002), total bilirubin (HR=2.17, p=0.009), aspartate-aminotransferase (HR=2.96, p<0.001), alanine-aminotransferase (HR=2.02, p=0.01) and γ -GT (HR=2.61, p<0.001). Absence of hypermetabolic lymph nodes was associated to a longer OS (HR=2.35, p=0.008), as well as a TLRMAA \geq 1.87 (HR=2.92, p=0.009). No other imaging biomarkers were found to be associated with OS. Finally, OS was significantly higher in patients treated according to PM (HR= 2.52, p<0.001). Results of the multivariate analysis showed that Total Bilirubin, Aspartate-aminotransferase and γ -GT were statistically significant with p of 0.03, 0.006 and 0.01 respectively. The method of calculation of individual activity (BSA vs PM) was also statistically significant even if we adjusted for standard biological parameters (Total Bilirubin, Aspartate aminotransferase and γ -GT) with HR=2.26 and p=0.03. No difference in terms of clinical, biological and imaging biomarkers were observed between patients treated by BSA or PM. However, as expected, patients treated with PM had significantly higher lesion Dmean than patients treated with BSA (average-Dmean of 86Gy vs 38Gy, p<0.001).

Conclusions : Our results demonstrated that personalised SIRT improves outcome in refractory intra-hepatic cholangiocarcinoma treated with SIRT. And that several baseline biomarkers could be used for patient's stratification.

- O17 -

90Y-PET/CT-BASED DOSIMETRY AFTER SELECTIVE INTERNAL RADIATION THERAPY PREDICTS OUTCOME IN PATIENTS WITH LIVER METASTASES FROM COLORECTAL CANCER. H. Levillain (1), I. Duran Derijckere (2), G. Marin (2), T. Guiot (3), M. Vouche (4), N. Reynaert (3), A. Hendlisz (5), B. Vanderlinden (3), P. Flamen (2) / [1] Institut Jules Bordet, Brussels, Belgium, Nuclear Medicine, [2] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, Nuclear Medicine, [3] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, Medical Physics, [4] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, Radiology, [5] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, GastroIntestinal Unit Medical Oncology Clinic.

Introduction : Selective internal radiation therapy (SIRT) based on intra-arterial embolization of yttrium-90 (⁹⁰Y)-labelled microspheres is an established treatment of primitive or metastatic liver disease. Recent preliminary data indicated that post-SIRT dosimetry correlated with FDG-PET-based metabolic response assessment performed 6–8 weeks after SIRT. The feasibility of ⁹⁰Y imaging with PET in the hours following SIRT has recently been assessed as well as its quantitative performance. Therefore, post-SIRT dosimetry, if related to patient outcome, could become a valuable tool for early post-SIRT treatment adaptation.

Aim : To confirm that post-SIRT ⁹⁰Y-PET/CT- based dosimetry correlates with lesion metabolic response and to determine its relationship with overall survival (OS) in liver-only metastases from colorectal cancer (mCRC) patients treated with SIRT.

Methods : Twenty-four mCRC patients underwent pre/post-SIRT FDG-PET/CT and post-SIRT ⁹⁰Y-PET/CT. Lesions delineated on pre/post-SIRT FDG-PET/CT were classified as non-metabolic responders (total lesion glycolysis (TLG)-

decrease < 15%) and high-metabolic responders (TLG-decrease \geq 50%). Lesion delineations were projected on the anatomically registered 90Y-PET/CT. Voxel-based 3D dosimetry was performed on the 90Y-PET/CT and lesions' mean absorbed dose (Dmean) was measured. The coefficient of correlation between Dmean and TLG-decrease was calculated. The ability of lesion Dmean to predict non-metabolic response and high-metabolic response was tested and two cutoff values (Dmean-under-treated and Dmean-well-treated) were determined using ROC analysis. Patients were dichotomised in the "treated" group (all the lesions received a Dmean > Dmean-under-treated) and in the "under-treated" group (at least one lesion received a Dmean < Dmean-under-treated). Kaplan-Meier product limit method was used to describe OS curves.

Results : Fifty-seven evaluable mCRC lesions were included. The coefficient of correlation between Dmean and TLG-decrease was 0.82. Two lesion Dmean cutoffs of 40 Gy (sensitivity 80%, specificity 95%, predictive-positive-value 86% and negative-predictive-value 92%) and 60 Gy (sensitivity 70%, specificity 95%, predictive positive-value 96% and negative-predictive-value 63%) were defined to predict non-metabolic response and high-metabolic response respectively. Patients with all lesions Dmean > 40 Gy had a significantly longer OS (13 months) than patients with at least one lesion Dmean < 40 Gy (OS = 5 months) (p = 0.012; hazard-ratio, 2.6 (95% CI 0.98–7.00)).

Conclusions : Our results demonstrates that, in chemorefractory mCRC patients treated with SIRT, lesion Dmean determined on post-SIRT 90Y-PET/CT correlates with metabolic response and higher lesion Dmean is associated with prolonged OS.

- O18 -

25 YEARS OF THE BELGIAN FAMILIAL ADENOMATOUS POLYPOSIS ASSOCIATION: RESULTS AND LESSONS FROM A NATIONWIDE REGISTRY. D. Leonard (1), A. Wolthuis (2), K. Dahan (3), M. Renson (4), A. Delespesse (4), K. Sanctorem (4), C. Verellen-Dumoulin (3), S. Laurent (5), K. Claes (6), D. Franchimont (7), S. Tejpar (8), A. D'hoore (2), E. Van Cutsem (8), A. Kartheuser (9) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Colorectal Surgery Unit, [2] UZ Leuven, Leuven, Belgium, Department of Abdominal Surgery, [3] Institut de Pathologie et de Génétique, Charleroi, Belgium, Institut de Pathologie et de Génétique, [4] Familial Adenomatous Polyposis Association, Brussels, Belgium, FAPA, [5] UZGent, Gent, Belgium, Department of Hepato-gastroenterology, [6] UZGent, Gent, Belgium, Center for Medical Genetics, [7] Erasme Hospital, Brussels, Belgium, Department of Gastroenterology, [8] UZ Leuven, Leuven, Belgium, Department of Oncology, [9] Cliniques universitaires Saint-Luc, Brussels, Belgium, Colorectal Surgery Unit.

Introduction : Familial Adenomatous Polyposis (FAP) is a hereditary syndrome characterized by the early development of numerous colorectal adenomas and different benign or malignant extra-colonic manifestations. Without prophylactic colectomy, all patients will develop colorectal cancer prematurely. The Belgian Familial Adenomatous Polyposis Association (FAPA) was founded in 1993 with the aim of registering familial adenomatous polyposis (FAP) patients, to provide education and support to those patients and to enable patient's surveillance, family screening and research through a national registry.

Aim : The aim of the present study was to present the long-term results of a nationwide FAP registry in terms of survival, incidence of cancer and surgical management.

Methods : The Belgian FAPA registry was established by collecting information on probands and construction of their pedigrees. Family members at risk were offered prophylactic endoscopic and molecular genetic examination. Data from all patients prospectively included in the registry between 1993-2018 were analysed.

Results : There were 442 patients from 199 families with a median age of 47 (2-88) and a median age at diagnosis of 23.5 (1-69) years. Out of 341 patients, 296 (87%) were tested positive for APC gene and 15 (4.3%) presented MUTYH associated mutations. A median number of 1 (1-7) desmoid tumors, mostly intra-abdominal, were present in 78 (18%) patients at a median age of 31 (2-77) years. Upper GI cancer was diagnosed at median age of 57 (22-83) years in 36 (8.1%) of the patients mainly localized in the duodenum (78%). Colorectal cancer was diagnosed in 100 (22.6%) patients at a median age of 43.5 (15-72) years and was distributed amongst 62/159 (39%) probands versus 38/283 (13%) call-up patients (p<0.001). The cumulative crude survival was 87% in call-up patients compared with 79% in probands (p=0.0209). A comparison of two diagnostic periods, before and after 1990, demonstrated a decreased prevalence of colorectal cancer from 24% to 22% (p=0.0003). Restorative proctocolectomy (RPC) was performed in 204 (52%) of the patients and total colectomy with ileo-rectal anastomosis (IRA) in 148 (38%). Of the latter, 22% underwent further secondary proctectomy. Over the study period the rate of RPC significantly increased compared to IRA (p<0.001). Median age at operation was 26 years.

Conclusions : Since the establishment of the Belgian Polyposis Register, centralized registration with identification and prophylactic examination of relatives at risk results in a substantial improvement of the prognosis.

- O19 -

THE METABOLIC CLINICAL RISK SCORE (MCRS) AS A NEW PROGNOSTIC MODEL FOR SURGICAL DECISION IN PATIENTS WITH COLORECTAL LIVER METASTASES. I. Duran Derijckere (1), H. Levillain (1),

A. Bohlok (2), C. Mathey (3), J. Nezri (2), R. Muteganya (3), V. Lucidi (4), F. Bouazza (2), G. Van Simaey (3), S. Goldman (3), A. Hendlisz (5), P. Flamen (1), V. Donckier (2) / [1] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, Nuclear Medicine, [2] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, Surgical Oncology, [3] C.U.B. Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium, Nuclear Medicine, [4] C.U.B. Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium, Abdominal Surgery, [5] Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium, Digestive Oncology.

Introduction : Accurate patient selection for curative intended surgery in with colorectal liver metastases (CRLM) remains challenging as predictive clinicopathologic factors and scores lack prognostic accuracy. We hypothesized that metabolic characteristics of CRLM, evaluated by [18F]-fluorodeoxyglucose Positron Emission Tomography / Computed Tomography (18FDG-PET/CT) could contribute to better characterization of tumor biology and improve surgical selection.

Aim : To evaluate if metabolic baseline characteristics of CRLM assessed with 18FDG-PET/CT at the time of diagnosis, before any preoperative treatment, could predict the benefit of surgery and furthermore to evaluate the impact of combining these metabolic data with standard Clinical Risk Score (CRS).

Methods : In a series of 450 patients operated for CRLM, we retrospectively identified two groups 1) long-term survival group (LTS), as defined by postoperative recurrence-free survival (RFS) ≥ 5 years, i.e. the patients who benefited of surgery, and 2) early relapse group (ER), as defined by RFS < 1 year, i.e. the patients who did not benefit of surgery. Patients in whom 18FDG-PET/CT performed at the time of diagnosis of CRLM before any preoperative treatment, was available were included, leading to 23 patients in the LTS group and 30 in the ER group. Clinicopathologic characteristics, CRS and baseline 18FDG-PET/CT metabolic parameters were compared between LTS and ER groups. Low and high-risk CRS were defined by scores of 0 to 2 and 3 to 5, respectively. Metabolic CRS (mCRS) was implemented, using 1 additional point to the standard 5-points CRS when the highest tumor standardized uptake value (SUV_{max}) and normal liver mean SUV (SUV_{mean(liver)}) ratio was > 4.3 . Low and high-risk mCRS were defined by scores of 0 to 2 and 3 to 6, respectively.

Results : No difference was observed between LTS (n=23) and ER (n=30) groups for clinicopathologic parameters, CRS and rates of low/high risk CRS. Median SUV_{max}/SUV_{mean(liver)} ratio was significantly increased in the ER versus LTS, respectively of 4.2 and 2.8 (p=0.008). mCRS was significantly different between LTS and ER groups (p=0.024), while 61% of the LTS patients had a low-risk mCRS and 73% of the ER patients had a high-risk mCRS (p=0.023).

Conclusions : Baseline 18FDG-PET/CT tumor characteristics appear of prognostic value in patients undergoing surgery for CRLM. mCRS may represent a new prognostic model to improve selection for surgery in these patients.

BELGIAN PANCREATIC CLUB (BPC)

- P01 -

PANCREATIC BLUNT TRAUMA IN CHILDREN: OBSERVATIONS FROM A MONOCENTRIC PILOT STUDY. G. Sonnino (1), P. Deprez (2), A. Pire (3), F. Zech (4), R. Reding (3), F. Smets (1), X. Stephenne (1), E. Sokal (1), I. Scheers (5) / [1] Université Catholique de Louvain, Brussels, Belgium, Pediatric Gastroenterology, Hepatology and Nutrition, [2] Université Catholique de Louvain, Brussels, Belgium, Gastroenterology and Hepatology, [3] Université Catholique de Louvain, Brussels, Belgium, Pediatric Abdominal Surgery and Transplantation, [4] Université Catholique de Louvain, Brussels, Belgium, Internal medicine, [5] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Pediatric gastroenterology, hepatology and nutrition.

Introduction : Pancreatic trauma is the fourth most frequent cause of abdominal trauma in children. Few studies focused on the impact of trauma severity and therapeutic management (surgery vs endoscopy vs observation) on mid- and long-term outcomes.

Aim : The aim of this study was to determine the mid and long-term morbidities related to the grade and the initial management of pancreatic trauma in children.

Methods : The charts of 29 children aged 0-<18 years admitted at The Cliniques Universitaires St Luc between 01/2007 and 01/2017 for an abdominal trauma involving the pancreas were retrospectively reviewed. Data about trauma characteristics, clinical symptoms, imaging, therapeutic management and short to long-term complications were recorded.

Results : We identified 29 patients (18/29, 62% boys) aged 2-17 years (median: 6.9y). Most children (18/29, 62%) had a mild pancreatic trauma (AAST grade I-II), while 11 had more severe (grade III-IV) pancreatic lesions. In 22/29 (76%) patients, pancreas trauma was associated to another organ lesion, liver injury being the most prevalent (17/22, 77%). Clinical symptoms are nonspecific to diagnose pancreatic involvement: pain (27/29, 93%) and nausea/vomiting (15/29, 52%). Imaging by CT-scan suspected ductal involvement in 90% of grade III-IV traumas. Five children were managed by endoscopy (3/5 grade III, 2/4 grade IV), 3 (3/3 grade IV injuries) patients had surgical management (2 by pancreaticojejunostomy and 1 for percutaneous drainage), while the other children were managed conservatively. Hospital stay was significantly shorter in grade I compared to the more severe grades (13 vs 19.5 days, $p = 0.025$). Mediate complications of pancreatic trauma consisted of pseudocysts; these were exclusively seen in grade III (5/5, 100%) and IV (4/5, 80%) traumas. Endocrine and exocrine pancreatic function was followed (median follow-up: 20.3 months) in 9/11 and 7/11 patients respectively with grade III-IV traumas. Endocrine function was preserved in all of them. Instead, exocrine function was impaired in 3/7 (43%); all of them complained of intermittent symptoms of abdominal pain and steatorrhea.

Conclusions : This monocentric study showed that compared to grade I-II pancreatic traumas, children admitted for pancreatic blunt injury grade III-IV had a higher risk of pseudocysts, required longer hospitalisation and more frequent re-hospitalisation for pancreatic reasons, and were more likely to evolve to exocrine pancreatic dysfunction over time. Follow-up of patients with grade III-IV-V pancreatic trauma is thus important to detect mid and long-term complications. Extending this study to a multicentric study will better enable us to analyse the effect of operative vs endoscopy vs observation management on the long-term outcome of these patients.

- P02 -

NECROTIZING PANCREATITIS: CAN MRI DIFFUSION-WEIGHTED IMAGING HELP IN DETERMINING INFECTION? M. Fernandez (1), M. Arvanitakis (1), M. Pezzullo (2), F. Jacobs (3), J. Devière (1), M. Delhaye (1) / [1] Erasme Hospital, Brussels, Belgium, Gastroenterology, Hepatopancreatology and Digestive oncology, [2] Erasme Hospital, Brussels, Belgium, Radiology, [3] Erasme Hospital, Brussels, Belgium, Infectious Diseases.

Introduction : Acute pancreatitis is a common disease worldwide, with the majority of patients having a rapidly favorable outcome. Nevertheless, 20% will develop moderate to severe disease with a high risk of infection of necrosis and organ failure; in these cases mortality can reach 15%. Infected necrosis requires management with antibiotics and invasive interventions. However, differentiating sterile from infected necrosis can be challenging. Diffusion-weighted magnetic resonance imaging (DWI-MRI) has shown promising results regarding the presence of infection or not in pancreatic pseudocysts. These results have not been generalized to pancreatic necrosis or walled-off necrosis (WON). On the other hand, there is limited data regarding microbiology and antibiotic use in these patients.

Aim : The aim of the study is to assess the diagnostic potential of DWI-MRI to detect infected necrosis, as well as determining the microbiology and antibiotic use in patients with necrotizing pancreatitis.

Methods : This is a retrospective study on patients with necrotizing acute pancreatitis admitted from 2010-2018, having undergone invasive interventions and MRI before intervention. Patients with chronic pancreatitis were excluded. Microbiology results based on fluid collected during drainage and sequential antibiotic use were recorded. Gold standard for an infected collection was considered when the culture of fluid collected during the initial drainage was positive. MRIs were reviewed and infection of the necrosis or WON was considered in case of a restricted diffusion signal.

Results : Thirty-nine patients were identified. The majority (59,5%) were men, and the main eti-ology was alcoholic in 15/39 (38.4%). Intensive care unit admission was required for 21/39 (53.8%) who presented with organ failure for a median duration of 7 (1-38) days. Median hospital stay was 70 (15-153) days. All patients had, at least, one endoscopic drainage (overall 2(1-7)). Endoscopic necrosectomy was required in 15/39 (38%) and combined percutaneous drainage in 12 (30.7%). Cultures collected during the first drainage were positive in 32/39 patients (82%). Microbiology results revealed more frequently gram-negative rods (ex E.Coli, Klebsiella Pneumonia and Pseudomo-nas). All patients were treated with antibiotics with a median duration of 43 (1-137) days, with 3 (0-12) adaptations according to clinical evolution or further bacteriological findings. Mortality during the initial hospitalization occurred in 7/39 (17.9%) patients. DWI-MRI was performed in 33 patients; sensitivity of DWI-MRI to detect infection was 75% and specificity 80%. CT revealed air bubbles in 8 patients; sensitivity and specifici-ty of this sign was respectively 26% and 100%.

Conclusions : DWI-MRI is a promising tool to distinguish between sterile and infected necrosis. Anti-biotics are overused in patients with necrotizing acute pancreatitis with suspected in-fection.

- P03 -

EUS-FNA/FNB ACCURACY AND OTHER QUALITY INDICATORS IN TWO ACADEMIC ENDOSCOPY CENTRES. M. Figueiredo Ferreira (1), M. Arvanitakis (1), A. Zaarour (2), E. Toussaint (1), J. Devière (1), J. Van Laethem (1), M. Gomez-Galdon (3), L. Verset (4), P. Demetter (4), P. Eisendrath (2) / [1] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Gastroenterology, [2] Saint-Pierre University Hospital, Brussels, Belgium, Gastroenterology, [3] Saint-Pierre University Hospital, Brussels, Belgium, Anatomopathology, [4] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Anatomopathology.

Introduction : Current literature defends EUS-guided sampling high accuracy, but discrepancies between cytological and surgical diagnoses are still observed. The clinical effectiveness of this technique seems to depend on its judicious use. New guidelines about technical and quality parameters in EUS performance have recently been published by the ESGE (European Society of Gastroenterology Endoscopy).

Aim : To monitor the quality indicators and determine the diagnostic accuracy of EUS-guided sampling in our facilities.

Methods : We performed a retrospective review of 170 cases of pancreatic solid lesions evaluated by EUS-guided sampling, between July 2015 and June 2018, in the Department of Gastroenterology of two academic tertiary-care centres (Hôpital Erasme and Hôpital Saint-Pierre), in Brussels. Cytological and surgical diagnoses were categorized into five groups: benign, malignant, suspect of malignancy, undetermined and insufficient for diagnosis. In patients who were not submitted to surgery, outcome was based on clinical evolution after 6 months of follow-up.

Results : Patients mean age was 63.3 year old (ranging from 24 to 89 year old) and 57.6% of patients were male. FNA-sampling was performed in the great majority of cases (92.1% FNA against 7.9% FNB), with a clear preference for the 22G needle (62.9%). Rapid on set pathological exam (ROSE) was performed in 48.8% of cases with 95% of agreement with definitive cytology. Cytology was considered insufficient to diagnosis in three cases, which means that the frequency of obtaining full diagnostic tissue sample was 98.2% (>90%, ESGE target standard). Also, nineteen patients were lost in follow-up. Subsequently, 148 cases with satisfactory yield in cytology specimens were statistically analysed and compared to surgical or clinical diagnosis. Of those, only 54 patients had a surgical resection. In comparison to surgical diagnosis, cytological results were true positive in 48 cases (89%), true negative in 3 cases (5.5%), false positive in 2 cases (3.7%) and false negative in 1 case (1.9%). False positive cases were both FNA samples, executed by two different endoscopists and one same pathologist, using 22G and 25G needles each. In both cases, ROSE was negative for malignancy, but cytological analysis (cell block) was suggestive of adenocarcinoma. Post-surgery histological results revealed an autoimmune pancreatitis and a chronic pancreatitis, respectively, with no signs of tumour. Non-malignancy was confirmed by long-term follow-up in both cases. When compared to surgical and clinical outcomes together, EUS-guided sampling sensitivity was 97.4% (95% CI, 92.6-99.5%), specificity was 96.9% (95% CI, 83.8-99.9%), positive predictive value was 99.1% (95% CI, 94.3 – 99.9%), negative predictive value was 91.2% (95% CI, 77.2-96.9%) and accuracy was 97.3% (95% CI, 93.2-99.3%). Chronic pancreatitis was present in 18.8% of cases. Post-procedural acute pancreatitis was reported in 3 patients (2%). There were no other EUS-sampling related complications.

Conclusions : The results of this retrospective analysis of EUS-guided sampling in our institution are comparable to previous published results and performance for diagnostic tissue sampling is well above ESGE proposed target standard of 90%.

- P04 -

AN UNUSUAL FINDING IN A PATIENT WITH ACUTE PANCREATITIS: CONGENITAL ANOMALY AS A CAUSE? L. Jongman (1), W. Kwanten (2), S. Van Outryve (2), S. Vyt (3), P. Steger (2) / [1] GZA, Wilrijk, Belgium, Gastroenterology and Hepatology, [2] GZA Sint-Vincentius ziekenhuis, Antwerpen, Belgium, Department of

Gastroenterology and Hepatology, [3] GZA Sint-Vincentius ziekenhuis, Antwerpen, Belgium, Department of Radiology. Several different developmental malformations of the pancreas have been reported in the literature, of which agenesis of the dorsal pancreas is a very rare entity. Nonetheless they should be sought for in young patients with pancreatitis without any other risk factors, especially when recurrent acute pancreatitis occurs. We report a case of acute pancreatitis due to a pancreas divisum with agenesis of the dorsal pancreas in a 32-year-old woman. This patient, with a history of gestational diabetes (but otherwise healthy), presented at the emergency department of our hospital with complaints of nausea and epigastric pain present for one day. This pain irradiated to the back and to the retrosternal space. She reported drinking only limited amounts of alcohol on occasions. She was a non-smoker. The physical examination revealed abdominal tenderness in the epigastric region, whereas the remaining clinical examination was normal. Biochemical evaluation of the patient revealed an elevated white blood cell count of 11.000/mm³ (normal values 3500-9800/mm³), a lipase of 3528 U/L (normal values <78 U/L) and a C-reactive protein of 41 mg/L (normal values <6 mg/L). The liver enzymes were within the normal range. The diagnosis of acute pancreatitis was made. Her present medical history reported no trauma or drug abuse. Lab results of triglycerides, calcium and immunoglobulin G4 (IgG4) were normal. Subsequential investigations showed the absence of biliary lithiasis, though presence of a hyperechogenic structure in the head of the pancreas and the presence of free abdominal fluid. Additional magnetic resonance cholangiopancreatography (MRCP) was performed and showed drainage of the main pancreatic duct in the minor papilla (as seen with pancreas divisum), whereas the body and the tail of the pancreas were absent (agenesis of the dorsal pancreas). This rare congenital anomaly was held responsible as cause for the acute pancreatitis, as it occurs in 30% of the patients with this finding. The exact mechanisms by which this anomaly causes pancreatitis are currently unknown. There were no arguments for polysplenia or other congenital anomalies of the cardiovascular or cerebral system, that are often associated with dorsal pancreas agenesis. Also, additional genetic testing for the pancreatic-duodenal homeobox 1 (Pdx1) gene and the pancreas transcription factor 1 subunit alpha (PTF1A) gene, associated gene-mutations, were negative in this patient. Our patient improved quickly after symptomatically treatment of pancreatitis that included intravenously fluid substitution and analgesics. There were no clinico-anamnestic arguments for exocrine pancreas insufficiency, nor was the oral glucose tolerance test (OGTT) deviant from normal.

- P05 -

RARE RETROPERITONEAL TUMOR DIAGNOSED BY EUS-GUIDED FINE NEEDLE ASPIRATION. L. Bromberg (1), M. Delhaye (2), J. Closset (3), L. Verset (4), M. Arvanitakis (2) / [1] Erasme Hospital, Brussels, Belgium, gastroenterology, [2] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, gastroenterology and hepatology, [3] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Surgery, [4] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, anatomopathologie.

A fifty-year old woman presented with abdominal pain in the upper left quadrant. Her medical history revealed diabetes and high blood pressure. During a work up two years earlier, a pancreatic mass was identified. Magnetic resonance imaging (MRI) revealed that the mass was extrapancreatic (18x31 mm). An endoscopic ultrasound (EUS) characterized the mass as hypoechogenic and hypervascularized. Fine-needle aspiration (FNA) was not contributory. Serum lipases, liver enzymes, CEA, CA 19-9 and chromogranin levels were normal. The presumed diagnosis was that of an accessory spleen. The patient underwent a new MRI in 2017. The pancreatic mass had increased in size (47x44 mm). The PET/CT showed moderate metabolic activity in the mass. The patient is referred to our institution for a complementary work-up. A scintigraphy with nanocolloid radiolabeled with ^{99m}Tc was not in favor of an accessory spleen. A second EUS revealed a 50mm extra-pancreatic mass 5 cm without invasion of the adjacent vascular structures. FNA revealed cytology suggesting hemangiopericytoma (HPC). The patient was addressed for surgical resection. HPC is a rare soft tissue sarcoma, mostly described in the central nervous system. It is associated with aggressive prognosis and a tendency to metastasis or recurrence. Exceptional cases of HPC arising outside of the central nervous system including liver, gastrointestinal tract, retroperitoneum, have been reported. No typical CT findings have been reported for HPC. The first choice of treatment for HPC is wide surgical excision. Local recurrence rates up to 90% and metastatic rates up to 33% have been reported.

BELGIAN WORKING GROUP ON DIGESTIVE PATHOLOGY

- R01 -

PROGNOSTIC SIGNIFICANCE OF CDX2 EXPRESSION IN RESECTED STAGE II AND STAGE III COLORECTAL CANCER. M. De Pelsemaeker (1), M. Van Den Eynde (2), A. Kartheuser (3), P. Baldin (4), A. Jouret-Mourin (4) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, Department of Pathology, [2] Cliniques universitaires Saint-Luc, Brussels, Belgium, Department of Gastroenterology and Oncology, [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Department of Abdominal Surgery and Transplantation, [4] Cliniques universitaires Saint-Luc, Brussels, Belgium, Department of Pathology.

Background : The absence of CDX2 expression in stage II and III resected colon cancer has been shown as a poor prognosis factor, which could justify adjuvant chemotherapy in CDX2-negative stage II tumors. This assessment was based on a dichotomist -presence versus absence of CDX2 immunoeexpression (on tissues microarrays) (1). (1) Dalerba et al : CDX2 as a Prognostic Biomarker in Stage II and Stage III Colon Cancer, The New England Journal of Medecine (January 21,2016) Vol.374 No.3

Aims : (i) To score CDX2 immunoeexpression by using immunohistochemistry on histological sections of surgical specimen resections. (ii) To assess the prognostic significance of CDX2 immunoeexpression in our cohort.

Methods : Methods: We performed a retrospective study including 80 patients with stage II or III colon or rectal tumors operated at the Cliniques universitaires St-Luc between the 01/01/2010 and 31/12/2012. CDX2 immunoeexpression was evaluated on the most representative slide section of each patient. Clinico-pathological informations were available for the analyses. Comparisons were made using the Mann-Whitney test. Cumulative Relapse-Free Survival (RFS) and Overall Survival was performed using the Kaplan-Meier estimator and compared by log-rank tests. Cox regression we used for uni- and multi-variate analysis. P value of less than 0.05 was considered statistically significant.

Results : Results: The mean age of our cohort reached 70+/-13.63 years. Tumors were localized in the rectum (38,8%), in proximal colon (27,5%), and in distal colon (33,8%). 6,3% were of the mucinous type, 5% were well differentiated, 61,3% were moderately differentiated and 27,5% were poorly or undifferentiated. We identified 3 patterns of CDX2 immunoeexpression: (i) positive (intense and diffuse) in 50 cases (62,5%), (ii) heterogeneous in 17 cases (21,2%), and (iii) absent in 13 cases (16,3%). We observed a significantly higher 5-year OS rate (80% vs 50%) and 5-year RFS rate (23,3% vs 12%) in the CDX2-positive group compared to other CDX2 patterns. Analyzing each pattern individually, CDX2-heterogeneous pattern had also a lower 5-years OS rate (44,4% vs 82,1%) compared to CDX2-positive pattern. The non-positive CDX2 patterns had the worst prognosis and were significantly associated with female sex, tumor invasion, tumor size, lymphatic spread and undifferentiated tumor.

Conclusion : We identified different patterns of CDX2 expression with different prognostics and clinico-pathological feature association. Our data confirm that CDX2-negative and suggest that CDX2-heterogeneous patterns are both associated with poor prognosis.

- R02 -

CASE REPORT: CO-EXISTENCE OF SERRATED ADENOMA AND ADENOCARCINOMA EX GOBLET CELL CARCINOID IN THE APPENDIX. F. Cordier (1), L. Ferdinande (2), W. Willaert (3), A. Hoorens (2) / [1] University Hospital Gent, Belgium, Pahtology, [2] University Hospital Gent, Belgium, Pathology, [3] University Hospital Gent, Belgium, Surgery.

We present the case of a 62-year-old man, with a history of ulcerative colitis, who presented with acute abdominal pain, from low abdominal to the right flank. A blood analysis revealed an elevated CRP (22 mg/L). An abdominal ultrasound demonstrated an enlarged appendix, but an expected approach was chosen. The pain spontaneously diminished. After a week, a new abdominal ultrasound was performed that could not visualize the appendix. CT abdomen showed an enlarged appendix without signs of peri-appendicular infiltration, suggesting a chronic appendicitis with dilatation. A laparoscopic appendectomy was performed. On gross examination, the appendix was dilated at the tip. On cut surface, there was a narrow lumen more proximally and the dilated tip was filled with mucin. The base of the appendix showed no macroscopic abnormalities. Microscopic evaluation showed that the mucosa at the tip was lined with a proliferation of mucinous epithelial cells, growing in slender villi with scant lamina propria. The muscularis mucosae was intact. In the underlying appendiceal wall, however, an infiltrative tumor with two components was recognized near the narrowed lumen. One component showed small nests of signet-ring-like cells, staining for chromogranin A and synaptophysin. The second component was composed of mucin pools containing floating layers of columnar tumor cells and nests of signet ring cells. The invasive mucinous tumor component showed perforation of the serosal layer with mucin and tumor cells outside the appendix. The diagnosis of both a serrated adenoma and adenocarcinoma ex goblet cell carcinoid (adexGCC) was made. As the proximal resection margin was invaded by tumor, the patient subsequently underwent

right hemicolectomy and debulking surgery with HIPEC with detection and resection of a peritoneal metastasis. The co-existence of a serrated adenoma and adexGCC was only rarely described in literature. This case illustrates the importance of thorough sampling of appendectomy specimens, especially in the presence of macroscopic abnormalities.

- R03 -

MESOTHELIAL-TO-MESENCHYMAL TRANSITION IN THE PATHOGENESIS OF COLORECTAL PERITONEAL METASTASES. J. Demuytere (1), W. Ceelen (2), J. Van Dorpe (3), A. Hoorens (3) / [1] Ghent University, Ghent, Belgium, Faculty of Medicine, [2] University Hospital Gent, Belgium, Department of Gastrointestinal Surgery, [3] University Hospital Gent, Belgium, Department of Pathology.

Introduction : The perception of the role of the peritoneal microenvironment in the pathogenesis of peritoneal carcinomatosis (PC) has shifted from viewing the peritoneal monolayer as a passive barrier to implicating mesothelial cells as important actors in metastasis. Recent insights regarding mesothelial cells and their interactions with cancer cells have implicated the process of mesothelial-to-mesenchymal transition (MMT) as a mechanism by which mesothelial cells can transdifferentiate into cancer-associated fibroblasts (CAFs) in several cancers metastasizing to the peritoneum. MMT might prove to be a common disease mechanism in peritoneal metastasis. However, its role in recruiting CAFs in colorectal cancer (CRC) has not been evaluated extensively.

Aim : To examine the presumed mesothelial origin of these CAFs in three histopathological variants of colorectal carcinoma, including conventional type adenocarcinoma, mucinous carcinoma and signet ring cell carcinoma.

Methods : We evaluated the expression of mesothelial, mesenchymal, angiogenesis and CRC-related markers in peritoneal surgical residual tissue of twelve CRC-patients with PC (five conventional type adenocarcinomas, four mucinous carcinomas, and three signet ring cell carcinomas) and four control patients by means of immunohistochemistry. Immunofluorescent double staining was performed using podoplanin and fibroblast activating protein (FAP)- antibodies.

Results : We observed morphological and immunohistochemical changes in the vicinity of tumor implants in all three studied colorectal cancer variants, but we observed several differences between them. In all variants, mesothelial cells acquired a spindle-shaped myofibroblast-like morphology, lost expression of mesothelial markers and gained expression of mesenchymal markers. Analysis of consecutive tissue sections for mesothelial and mesenchymal markers revealed overlap in expression of the mesothelial markers WT1 (Wilms' tumor-1 protein) and podoplanin and the CAF marker FAP (fibroblast activating protein). Immunofluorescent double staining of a representative sample was able to confirm the overlapping expression of podoplanin and FAP in CAFs. Samples of mucinous carcinoma and signet ring cell carcinoma exhibited less activation of the peritoneal surface, although all variants recruited a large number of CAFs.

Conclusions : Taken together, both the observed changes in expression pattern and morphological changes in mesothelial cells are highly suggestive of a mesothelial origin of CAFs in the peritoneal microenvironment of colorectal cancer metastases. Interfering with the process of MMT might prove to be a valuable approach in treating and preventing PC in CRC. Differences observed in different CRC variants suggest that one single strategy might not be applicable for all types of CRC.

- R04 -

ENDOSCOPIC FEATURES, PATHOLOGICAL CORRELATES AND POSSIBLE ORIGIN OF FOVEOLAR GASTRIC METAPLASIA PRESENTING AS A DUODENAL POLYP. L. Libbrecht (1), H. Dano (2), C. Toussaint (3), H. Piessevaux (3) / [1] Cliniques universitaires Saint-Luc, Woluwe-Saint-Lambert, Belgium, pathology, [2] Saint-Luc University Hospital, Brussel, Belgium, Department of Pathology, [3] Saint-Luc University Hospital, Brussel, Belgium, Department of Gastroenterology.

Introduction : It has recently been shown that duodenal foveolar gastric metaplasia (FGM) sometimes presents as a polyp. The mechanism by which FGM develops into a polypoid lesion is unknown and it unclear whether this form of FGM is indistinguishable from other polypoid lesions or whether endoscopists do not recognize it because they are unfamiliar with it.

Aim : The current study aims to evaluate the endoscopic features of such polyps and to examine whether its pathological features can shed light on its pathogenesis.

Methods : We identified and retrieved archival cases of FGM endoscopically suspicious for adenomatous polyp and examined their pathological, clinical and endoscopic features

Results : Endoscopic features of the 13 identified FGMs presenting as polyps were heterogeneous and overlapping with those of adenomatous polyps. FGM was frequently associated with mucosal and submucosal Brunner's glands, but defining and recognizing hyperplasia of these glands remains difficult. Other pathological features could not explain the development of a polypoid lesion.

Conclusions : The endoscopic features of FGM polyps are non-specific, overlapping with those of adenomatous polyps. FGM polyps probably acquire their polypoid aspect due to association with Brunner's gland hyperplasia (BGH), which also arises due to chronic inflammation and damage. Because BGH is ill-defined and difficult to recognize, while FGM is diagnosed easily, this type of polypoid lesions has until now only been recognized based on the presence of FGM, although FGM is most likely a secondary phenomenon and not the primary cause of the polyp.

- R05 -

HEPATOCELLULAR ADENOMA, FOCAL NODULAR HYPERPLASIA AND HEPATIC GRANULOMAS IN ONE SINGLE PATIENT: A CURIOUS ASSOCIATION. R. Dehon (1), I. Scagnol (2), M. Komuta (3), P. Demetter (1), M. Gomez-Galdon (1) / [1] Institut Jules Bordet, Brussels, Belgium, Department of Pathology, [2] Centre Hospitalier Universitaire de Liège, Liège, Belgium, Department of Pathology, [3] Cliniques universitaires Saint-Luc, Brussels, Belgium, Department of Pathology.

Introduction : We report the case of a 30 years old woman with a hepatocellular adenoma (HCA), focal nodular hyperplasia (FNH) and hepatic granulomas. This association is rare and can lead to diagnostic difficulties.

Observation : The patient presented in the hospital for asthenia. Biological investigations revealed an increase in CRP and abnormal liver tests (elevation of gamma-glutamyl transferase and alkaline phosphatase). Abdominal ultrasonography and hepatic MRI showed a nodular subcapsular hepatic lesion in segment V. The lesion measured 73 x 69 mm and had an arterial-phase enhancing. The lesion presented radiological features in favour of a benign tumour, possibly an adenoma. It was decided to perform MRI control at 6 months. The patient stopped taking oral contraceptives known to be associated with liver cell adenoma. The MRI control showed a slowly growing lesion and revealed a second lesion in segments IV and VIII presenting comparable radiological characteristics. Both lesions were surgically removed. An orange-brown multinodular mass was found in segment V whereas segments IV and VIII contained a well circumscribed yellowish nodule. Histopathological examination showed a HCA in segment V and a FNH in segments IV and VIII. The HCA overexpressed C-reactive protein, which is consistent with an inflammatory subtype. Moreover, non-caseating epithelioid granulomas were seen in both liver lesions and in the surrounding liver parenchyma. The patient was not known with granulomatous disease.

Conclusion : Coexistence of HCA with FNH and hepatic granulomas is rare and confuses diagnosis. Long-term use of oral contraceptives can induce both HCA and FNH. Moreover, oral contraceptives are listed as one of many drugs known to cause hepatic granulomas. We propose that the hepatic granulomas in this case are a response to persistent inflammation caused by the (inflammatory) HCA and the FNH, a local response to the tumours, a consequence of contraceptives use, or a combination of these factors.

- R06 -

BELIEVE IT OR NOT: UNUSUAL PROGRESSION OF LIVER LESIONS. S. Gossé (1), B. Gys (2), T. Chapelle (2), B. Op De Beeck (3), A. Driessen (4), T. Vanwollegem (1), P. Michielsens (1), L. Vonghia (1), S. Francque (1) / [1] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Gastroenterology, [2] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Surgery, [3] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Radiology, [4] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Pathology.

We describe a case of a 65-year old women, diagnosed years ago with histologically confirmed steatohepatitis, most likely non-alcoholic. Transaminases are persistently mildly elevated (ALT>AST), as are gamma-GT and alkaline phosphatase. The patient has several criteria of the metabolic syndrome, including impaired glucose tolerance with hyperinsulinism, dyslipidemia, visceral fat accumulation and arterial hypertension. Despite complete abstinence of alcohol and weight loss, there was no normalization of liver biochemistry. In previous workup, MRI showed some millimetric hyperintense noduli with characteristics of biliary cysts or small hamartomas. In 2017 she was diagnosed with a ductal mamma carcinoma treated with resection and adjuvant radiotherapy. Recently, at the occasion of an ultrasound in the context of her NAFLD follow-up, the liver showed marked heterogeneity of its parenchyma and an irregular surface. Elastographic values were high, in the cirrhotic range. Liver biochemistry was also substantially more disturbed compared to previous values. Liver metastases were suspected. MRI showed a slightly enlarged liver with pseudocirrhosis due to miliary opacities. Differential diagnosis based on MRI included microabscesses, peliosis hepatis, miliary metastasis and diffuse hepatocellular carcinoma. In this oncological context, we referred our patient for a surgical excision biopsy (to avoid insufficient sampling for accurate diagnosis with a fine needle percutaneous biopsy). Macroscopic appearance of the liver showed diffuse greyish micronodularity. Histological exam confirmed the presence of multiple Von Meyenburg Complexes. Previous images were revised, confirming the earlier diagnosis of only few millimetric lesions and hence confirming the true and marked progressive nature of the lesions. Von Meyenburg Complexes (VMC) or bile-duct hamartomas are thought to be a benign entity and are a relatively common incidental autopsy finding, with a

prevalence of 2-5%. This congenital fibrocystic liver lesion results from the failure of involution of embryonic bile ducts. Histopathology is characterized by proliferation of bile ducts lined by normal-appearing epithelium set in a fibrous stroma that is frequently hyalinized. It is generally asymptomatic and considered as static. There are reports of VMC presenting with diffuse abdominal pain and discomfort, cholangitis and portal hypertension. Most authors believe that neoplastic transformation of bile-duct hamartoma does not occur. In recent years, a number of case reports showed that there is a possible association with intrahepatic cholangiocarcinoma. Histological malignant transformation in the sequence of hyperplasia – metaplasia - dysplasia can be seen near this VMC. However, concomitant liver diseases as hepatitis, cirrhosis and hemochromatosis can be predisposing factors in the development of cholangiocarcinoma. In this case, which is exceptional because of its marked progressive nature with rather rapidly evolving diffuse lesions on imaging, careful follow-up is warranted.

- R07 -

WHITE TUMOR IN THE COLON. Z. Issa (1), C. Debaille (1), M. Mignon (2), D. Augusto (3), G. Catala (4), M. Schapira (1) / [1] Centres Hospitaliers Jolimont, Belgium, Hepato-gastro-enterology, [2] Centres Hospitaliers Jolimont, Belgium, Interventional radiology, [3] Centres Hospitaliers Jolimont, Belgium, Anatomopathology, [4] Centres Hospitaliers Jolimont, Belgium, Oncology.

Colorectal cancer is the most common cancer of the gastrointestinal tract, the third most frequent malignancy in the world and the third cause of death due to cancer. However, not all colorectal cancers derive from the colon and sometimes the pathologist gives us a surprisingly different diagnosis. We present the case of a woman with a white tumor in the colon that turned out to be an unusual lesion of another origin. A 63 years-old woman was addressed for a sigmoidoscopy in order to investigate a hypermetabolic lesion in the sigmoid found on a PET scan done ten days earlier. She had history of appendectomy and right ovarian cystectomy. Her family history was negative for cancer. She took no medication, didn't smoke and had no alcohol consumption. A couple of months earlier, she started to notice a growing left parasternal mass with no underlying pain nor respiratory symptoms. She also had newly onset constipation without rectal bleeding nor abdominal pain. At physical examination, a left parasternal mass was palpated with no other abnormal findings. Blood tests showed a small degree of inflammation with no anemia, normal blood cells count, normal hepatic enzymes levels and normal renal function. She underwent a thoracic CT scan that confirmed the presence of a left parasternal mass associated with sternal lysis and signs of mediastinal involvement. No breast lesion was seen on the mammogram. That's when the PET scan was performed which highlighted the hypermetabolic activity of the left parasternal mass as well as another mass in the sigmoid associated with five lombo-aortic adenopathies. Abdominal CT showed circumferential thickening of the sigmoid over 12 cm in contact with a less well-defined right pelvic mass with signs of peritoneal carcinomatosis and aorto-iliac adenopathies. MRI of the pelvis confirmed the presence of a heterogenous right paramedian pelvic mass of 140x37x38mm that infiltrates the sigmoid. It also showed pelvic ascites and multiple peritoneal nodules. On sigmoidoscopy, at around 30 cm from the anal verge, the colonic mucosa had a hillocky aspect with several ulcerated « bumps » followed by a circumferential tumor-like lesion of white color with ulcers in its centre. Biopsies were taken. In the meanwhile, the left parasternal mass was biopsied under ultrasound guidance. Tumor markers were positive for CA15.3 (120 U/mL) and CA125 (3082 U/mL) and negative for CEA and CA19.9. Both lesions had similar anatomopathological characteristics showing an aspect of a poorly differentiated epithelial carcinoma with the following immunohistochemical profile : pancytokeratin positive, CK7 positive, PAX8 positive and CA125 positive while all other markers (P40, GATTA3, mammaglobin, TF1, chromogranin A, CD56, synaptophysin and melan A) were negative. Ki67 was at 95%. Based on this immunohistochemical profile, the diagnosis of metastatic ovarian cancer was made and the patient was addressed to our oncology department. Soon after, treatment with chemotherapy was initiated. Metastasis to the colon and rectum are rare and are considered to account for around 1% of all colorectal cancers. The three most frequent primary cancers responsible for colonic metastasis are lung cancer, ovarian cancer and breast cancer. Colonic metastasis of ovarian origin account for 4-6% of cases and the diagnosis is often made in a patient with a known history of ovarian cancer. Our case is unusual because colonic metastasis was synchronous to the initial diagnosis. Only a couple of similar cases are published in the literature. Moreover, our endoscopic finding is unique in its white nature (picture available) as previous papers described it as a polypoid lesion or an elevated irregular lesion with ulcers. Dissemination of ovarian cancer cells can happen by four different pathways; lymphogenous, hematogenous, by direct infiltration of the colonic wall or through the peritonium. The latest is thought to give the most suitable pathophysiological explanation. Finally, immunohistochemical evaluation with tumour markers is capital for identifying the origin of colonic metastasis as illustrated in our case. A CK7+/CK20- profile often signs a secondary colon malignancy while a CK7-/CK20+ profile is often found in primary colorectal malignancy.

- R08 -

CASE REPORT OF A KAPOSI SARCOMA INVOLVING THE UPPER DIGESTIVE TRACT IN A 40-YEAR-OLD KIDNEY TRANSPLANT PATIENT. M. Poncin (1), J. Loly (2), J. Belaiche (3), C. Bonvoisin (4), P. Honoré (5), J. Somja (6), S. Defroidmont (6), E. Louis (3) / [1] CHU de Liège, Liège, Belgium, Gastroenterologie, [2] CHU Liege,

Liège, Belgium, gastroenterology, [3] CHU Liege, Liège, Belgium, Gastroenterology, [4] CHU Liege, Liège, Belgium, Nephrology, [5] CHU Liege, Liège, Belgium, Abdominal Surgery, [6] CHU Liege, Liège, Belgium, Pathology.

Introduction : Dr M Kaposi first described Kaposi sarcoma in 1872. Since, five distinctive forms have been described: endemic African form, classic form (European), AIDS related, endemic Mediterranean, and iatrogenic due to immunosuppressant associated with organ transplant. It involves usually the skin system but multi-visceral lesions are commons. Gastro-intestinal tract is the most extra-cutaneous site affected (Lee AJ, 2015).

Case report : We report a case of gastrointestinal involvement of a Kaposi sarcoma in a 40-year-old immigrant man from Djibouti who lives in Belgium since 2011. The patient benefited from kidney transplant in august 2015. Initial kidney disease was undetermined. He is treated with tacrolimus 13mg, mycophenolate mofetil 2x0.75mg, and methylprednisolone 4mg He was first complain about nausea and vomiting in April 2017. As complains were sustainable, a first gastroscopy was performed in September 2017. Small purple sub-mucosal-flat lesions were described in fundus and antral area. Biopsies where performed but non contributive. A PETCT was then performed with demonstration of sus-clavicular adenopathies and a focal hyper-metabolic lesion of the third duodenum. A second gastroscopy was performed on December 2017 with a colonoscope to reach easily the third duodenum and the proximal jejunum. Multiples lesions where discovered with different pattern ranging from flat purple to ulcerated pseudo-polypoid or volcano-like lesions. Biopsies were performed again and show non - atypical spindle - shaped fusiform cells with no mitotic activity. Focally, there are lymphangiectasias. The lamina propria is locally infiltrated with lymphoplasmocytic inflammatory. The anti-HHV8 antibody test shows positivity in the majority of the tumour cells. Late December 2017 dermatologist found a small blue purple lesion on the nose evocating a skin involvement of a Kaposi sarcoma Nephrologist decided to reduce advagraft, discontinue MMF and introduce certican with bettering of the skin lesion. He's asymptomatic concerning the digestive sphere.

Discussion : In this report we present a case of Kaposi sarcoma with initial involving of the upper gastro-intestinal tract. A small skin lesion was found later. Kaposi sarcoma is a systemic disease that usually involves the skin at beginning but visceral lesions have been described without skin lesion. Gastro-intestinal tract is the most extra-cutaneous site affected (Lee AJ, 2015) (Parente F, 1991). The incidence of GE involving is variable but remain rare, ranging from less than 10% in non AIDS related form to 45% in AIDS related Kaposi. (Lee AJ, 2015) Stomach and small intestine lesions are more frequent than oesophageal or colonic lesions. (Kolios G, 1995) In a Portuguese cohort of 13 patients with upper GE tract involving, a colonoscopy was performed in a third (4/11) without any colonic lesion; (Carmo J, 2017) Lesion patterns can be multiple: reddish or purplish patchy lesions, polypoid/nodular, pseudo-tumoral or depressed and ulcerated (volvano-like) (Carmo J, 2017)) GE involving is not necessarily symptomatic. Symptoms that have been associated are nausea, diarrhoea, abdominal pain, intussusceptions, bleeding or perforation. In our case, KS happened in an immuno-compromised patient because of its kidney transplantation and anti-reject drugs inherent of this condition. It seems to be more frequent in renal transplant than other however some studies don't confirm these data. Furthermore, KS is more frequent in patients from areas where HHV-8 is endemic. Djibouti is en endemic country for HHV-8. In our case, HHV-8 antibody is positive in jejunum and skin specimen but PCR HHV-8 is negative on blood. So the diagnostic should be based on biopsy samples. In our cases, first biopsies were negative because of the sub-mucosal pattern of the disease. When a KS is suspected, multiple samples should be done trying to get focal sub-mucosal samples. In case of immuno-compromised patients, management consist in reducing anti-reject drugs. If not efficient, chemotherapy should be performed.

Conclusion : The initial involvement of the gastroenterology tract by a Kaposi Sarcoma can be a challenging diagnostic as it can be asymptomatic and when symptoms are present, they are totally non-specific. An upper GE endoscopy should be performed with repeated biopsy, involving sub-mucosal samples, if a patient is at risk from developing a Kaposi sarcoma. PETCT can help to reach the most representative lesion.

- R09 -

IN PATHOLOGY WE TRUST! OR SHOULDN'T WE? S. Van Langendonck (1), G. Van Parys (2), M. Cool (3), G. Lambrecht (3), G. Deboever (3) / [1] AZ Damiaan, Oostende, Belgium, Gastro-enterologie, [2] AZ Damiaan, Oostende, Belgium, anatome pathologie, [3] AZ Damiaan, Oostende, Belgium, Gastro-Enterologie.

A 63-year-old female patient consulted our outpatient clinic for a second opinion concerning therapy refractory ulcerative colitis. This was diagnosed last year based on endoscopy and pathology findings and she has been treated since then with 5-ASA suppositories and beclomathason tablets, without any improvement of the symptoms. Her past medical history included a hysterectomy, a cystopexy and a bipolar disorder. Her current complaints were rectal tenesmus, intermittent anal blood loss and fecal incontinence. The clinical abdominal examination was normal. On digital rectal examination the resting tone of the anal sphincter and the voluntary contraction were clearly reduced. The laboratory tests were normal, excluding a slightly elevated C-reactive protein at 7.2 mg/L (reference range <5). On proctosigmoidoscopy examination the rectal mucosa was clearly abnormal with an almost circular nodular conversion and elevated and congested folds covered with a fibrinopurulent exudate. The lesion extended from the lower rectum up to the proximal third, but the last 2-3 cm of the distal rectal mucosa were normal. Large macro-loop biopsies were taken and the pathology results showed

a preserved rectal mucosa with slightly elongated tortuous crypts and areas of mild erosion. The lamina propria was normal, only at the areas of erosion a slight inflammation was noted. The epithelial cells were covered with fibrinopurulent caps. There were no granulomata and the muscularis mucosae was normal. The pathologist concluded that these findings were consistent with CAP polyps and suggested the possibility of rectal mucosal prolapse. Although the patient didn't mention it spontaneously, upon specific questioning she confirmed to have a rectal protrusion while bearing down needing manual reduction. A defaecography was performed and showed indeed an important rectal prolapse grade V. We concluded that the rectal cap polyposis in this patient was caused by repeated mucosal trauma and ischemia due to straining and prolapse. We proposed her a surgical rectopexia and postoperative endoscopic follow-up. Cap polyposis is characterized endoscopically by multiple smaller or bigger polyps frequently located in the rectum and distal sigmoid and rarely spreading to the rest of the colon. Pathological examination shows inflammatory polyps with elongated tortuous crypts, whereby the surface is covered with a fibrinopurulent cap of exudate and granulation tissue. C-reactive protein and white blood cell counts are normally in reference range. The differential diagnosis includes inflammatory bowel disease, juvenile polyposis syndrome, colitis cystica profunda, nodular lymphoid hyperplasia and Cronkhite-Canada syndrome. In the case of rectal cap polyposis the most important differential diagnosis is ulcerative colitis. The etiology of cap polyposis is still incompletely understood. The rectal form is probably in most cases caused by mucosal trauma and ischemia which in turn is caused by straining and rectal prolapse. Elsewhere in the colon it is probably also caused by abnormal colonic motility with excessive straining and repeated mucosal trauma, as part of the mucosal prolapse syndrome. Other causes have been postulated as well, including inflammatory bowel diseases and even *Helicobacter pylori* positive gastritis, but the evidence supporting these hypotheses is lacking. Malignant conversion has never been reported and spontaneous healing has rarely been documented. In the literature there are case reports and small series of medical treatment with 5-ASA, topical steroids and even anti-TNF. The evidence supporting these treatments is very limited. Treatment for rectal cap polyposis should primarily be aimed at treating the underlying cause of straining, if possible conservative, if needed surgically in case of major prolapse. Surgical resection of the affected segments, as has rarely been reported, should be avoided. References 1. Williams GT, Bussey HJ, Morson BC. Inflammatory "cap" polyps of the large intestine. *Br J Surg* 1985; 72: S133. 2. Tomiyama R, Kinjo F, Kinjo N, et al. Gastrointestinal: cap polyposis. *J Gastroenterol Hepatol* 2003; 18:741. 3. Konishi T, Watanabe T, Takei Y, et al. Cap polyposis: an inflammatory disorder or a spectrum of mucosal prolapse syndrome? *Gut* 2005; 54: 1342-1343. 4. Akamatsu T, Nakamura N, Kawamura Y, et al. Possible relationship between *Helicobacter pylori* infection and cap polyposis of the colon. *Helicobacter* 2004; 9:651. 5. Tamura K, Matsuda K, Yokoyama S, et al. Successful laparoscopic resection for cap polyposis: case report, literature review. *Surgical case reports* 2018; 4:69.