-A13-

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

Introduction: In metabolic dysfunction-associated steatotic liver disease (MASLD), intrahepatic vascular resistance (IHVR) increases in early stages, driven by liver sinusoidal endothelial cell (LSEC) dysfunction and their loss of fenestrae (capillarisation). This phenomenon contributes to disease progression. The pan-peroxisome proliferator-activated receptor (pan-PPAR) agonist lanifibranor has demonstrated beneficial effects on liver histology in patients with MASLD and was also shown to have favourable effects in preclinical models of cirrhosis and portal hypertension. We previously demonstrated that lanifibranor normalised increased IHVR in a rat model of isolated steatosis by improving liver histology and primarily restoring both the structural and functional intrahepatic vascular alterations.
Aim: This study aimed to 1) explore ultrastructural sinusoidal remodelling across the human MASLD spectrum, 2) assess the effects of lanifibranor on LSEC fenestrae at histological and ultrastructural levels in a rat model of early MASLD, 3) and histologically evaluate the progression of LSEC capillarisation over time in a mouse model of MASLD.
Methods: Human liver biopsy samples (n = 13) across the full MASLD spectrum were evaluated by transmission electron microscopy (TEM). Male Wistar rats (n = 8/group) were fed a methionine-choline-deficient diet (MCDD) or control diet (CD) for 4 weeks and received simultaneously placebo or lanifibranor (100 mg/kg/day) via oral gavage QD. Rat livers were evaluated by CD34 immunostaining, TEM, and scanning electron microscopy (SEM) with quantitative analysis of fenestrae. Evolution of capillarisation over time was also explored by CD34 immunostaining in a second model using C57BL/6 mice (n = 6/group) fed either CD or a high-fat high-fructose diet (HFHFD) at 24, 36 and 44 weeks.
Results: On biopsies, non-MASLD liver displayed normal fenestrated sinusoids. Early MASL (F1-2) retained fenestrae but developed basement membrane fragments and perisinusoidal fibrosis. In steatohepatitis (F2-F3) LSEC thickening and loss of fenestrae occurred. Cirrhosis exhibited complete capillarisation. Placebo-treated MCDD-fed rats compared to CD-fed rats showed increased CD34 staining (38.8 ± 2.5 vs. 20.9 ± 2.8, $p < 0.001$), and ultrastructurally, increased fenestrae diameters, reduced fenestrae frequency (7.2 ± 0.4 vs. 10.8 ± 0.3, $p < 0.0001$) and LSEC porosity (5.7 ± 0.4 vs. 7.5 ± 0.2, $p < 0.01$). In MCDD-steatosis, lanifibranor decreased CD34 staining (21.4 ± 5.7 vs. 38.8 ± 2.5, $p < 0.05$) and restored fenestrae frequency (9.3 ± 0.3 vs. 7.2 ± 0.4, $p < 0.01$) and LSEC porosity (7.2 ± 0.3 vs. 5.7 ± 0.4, $p < 0.01$) to levels comparable with controls. In HFHFD-fed mice, CD34 staining increased with diet duration, reaching significant elevations at 36 and 44 weeks.
Conclusions: Across species, LSEC capillarisation develops early in MASLD, albeit heterogeneously, and progresses with disease severity. Lanifibranor restores LSEC (ultra)structure in early MASLD, highlighting its therapeutic potential to restore vascular alterations and beneficially influence disease progression.

-A14-

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

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Introduction: Immune-checkpoint inhibitors (ICIs) increasingly downstage hepatocellular carcinoma (HCC) to liver transplantation (LT), but their sustained immune activation may heighten the risk of graft rejection when given before or after transplant. Evidence remains limited to small and heterogeneous studies, suggesting higher rejection rates with short wash-out intervals. More data are needed to define safe timing and immunosuppression strategies around transplantation in ICI-exposed patients. Therefore, real-world multicentre data are needed.
Aim: We aim to evaluate the impact of immunotherapy on graft outcomes, the risk for rejection and post-transplant HCC recurrence.
Methods: We retrospectively collected data from patients treated with ICIs between January 2020 and October 2025 who underwent liver transplantation in all transplant centres in Belgium and in Beaujon Hospital, Paris. We collected demographic data, pre-transplant HCC characteristics (number and size of nodules, alpha-fetoprotein levels), and post-transplant outcomes.
Results: We collected data from 15 patients. The cohort consisted predominantly of men (80%), with a mean age at LT of 55.6 ± 12.3 years. Cirrhosis was mainly of viral origin (40%), and alcohol-related liver disease accounted for 20%. The mean MELD score was 12.1 ± 4.3, and most patients were classified as Child–Pugh A. The mean ALBI score was −2.2 ± 0.8. At HCC diagnosis, patients had on average 2.1 nodules, and the median size of the largest lesion was 55 mm (range 24–119). BCLC stage was B in most patients (80%), while two were classified as BCLC C and one as BCLC D. Mean alpha-fetoprotein at LT was 29.9 ng/mL. All but one patient received Atezolizumab plus Bevacizumab before LT. One patient received Durvalumab for a mixed HCC–iCCA lesion with predominant intrahepatic cholangiocarcinoma features. The median washout period between immunotherapy and LT was 5 months (range 1–23). The mean interval between HCC diagnosis and LT was 27.4 ± 19.6 months. Six patients (40%) underwent additional bridging therapies (radio- or chemoembolization, external radiotherapy, microwave ablation, etc.). On the liver explants (N = 12), 30% were classified as disease-free (pT0N0) and 30% as pT1 (a or b) N0. Two patients were pT2N0 and two were pT3N0. After a median follow-up of 10 months (range 1–32), two patients developed recurrence at 5.5- and 13-months post-LT, respectively. One patient had been classified as pT3N0 and the other as pT1bN0 with poorly differentiated HCC. The latter patient died from oncological progression despite salvage chemo and immunotherapy. Early allograft rejection within the first postoperative month occurred in two patients, both successfully treated with steroids. Among the 11 patients with available data on induction therapy, 8 received Basiliximab. Six patients are currently maintained on tacrolimus monotherapy without additional immunosuppressive agents.
Conclusions: Immunotherapy prior to liver transplantation appears feasible in carefully selected patients, with acceptable rates of rejection and early post-transplant outcomes. In our cohort, ICIs effectively contributed to tumour control and downstaging, enabling access to LT in patients with advanced HCC. However, longer follow-up and larger prospective studies are required to better assess the long-term risk of recurrence and to refine optimal timing and immunosuppression strategies in ICI-exposed candidates.

-A15-

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