PARIS
MASH
MEETING

2025 ABSTRACTS BOOK

11TH EDITION
SEPTEMBER 11 & 12 2025

INSTITUT PASTEUR

ABSTRACTS SUMMARY

ABSTRACTS SUMMARY

ABSTRACTS SUMMARY

ABSTRACTS SUMMARY

ABSTRACT N°1

TITLE: IS FIB-4 THE RIGHT TOOL FOR SCREENING FOR LIVER FIBROSIS?

AUTHORS

Leen Heyens, Hasselt University, Maastricht University, Ziekenhuis Oost-Limburg
Demi van Malde, MUMC+
Gediz Dogay Us, Maastricht University, Pax Clinic
Francesco Innocenti, Maastricht University
Mathieu Struyve, Ziekenhuis Oost-Limburg
Christophe Van Steenkiste, AZ Maria Middelares Ghent, Antwerp University Hospital
Sven Francque, Antwerp University Hospital, University of Antwerp
Geert Robaeys, Hasselt University
Ger Koek, MUMC+, Maastricht University
MASLD Research group, Hasselt University

KEYWORDS

MASLD, FIB-4, SCREENING

OBJECTIVES

The FIB-4 index showed poor agreement with VCTE and low sensitivity, making it an unreliable standalone diagnostic tool for liver fibrosis in people with MASLD in both primary and secondary care. Alternative non-invasive tests or improved cut-off values are needed for accurate fibrosis detection in clinical practice.

METHODS

A prospective cohort study (2019–2024) in Belgian and Dutch primary care used VCTE by FibroScan® (Echosens, France) as a proxy for the fibrosis stage. The FIB-4 index was derived from electronic patient data and study blood samples. A prospective cohort study (2019–2024) in Belgian and Dutch primary care used VCTE by FibroScan® (Echosens, France) as a proxy for the fibrosis stage. New fibrosis cut-offs (≥F2; ≥8kPa) for ≤65 and >65 years were determined via Youden's Index and validated in a Turkish primary care cohort and a Belgian secondary care type 2 diabetes mellitus (T2DM) cohort.

RESULTS

Among 563 participants (median age 62 years, 47.1% male, 14.2% with T2DM, median BMI 28.2 kg/m²), the agreement between FIB-4 and VCTE was low (κ = 0.138, 95% CI: 0.069–0.207). Suggested new cut-off values were 1.29 for individuals ≤65 years and 1.72 for those >65 years. The performance of the current cut-off value of 1.3 and the suggested 1.29 was very similar in both validation cohorts. For the cut-off value of 1.72, the sensitivity, specificity, PPV, and NPV were in the Turkish cohort, 66.7% (95% CI, 35.4-87.9), 67.2% (95% CI, 55.0-77.4), 22.2% (95% CI, 10.6-40.8), and 93.5% (95% CI, 82.5-97.8) and in the T2DM cohort the sensitivity, specificity, PPV, and NPV were 52.3% (95% CI, 37.9-66.2), 57.9% (95% CI, 42.2-72.1), 59.0% (95% CI, 43.4-72.9), 93.5% and 51.2% (95% CI, 36.8.0-65.4), respectively. In both the validation cohorts, the suggested cut-off value of 1.72 outperforms the current 2.0 value regarding sensitivity, but specificity is lower.

CONCLUSIONS

The FIB-4 index showed poor agreement with VCTE and low sensitivity, making it an unreliable standalone diagnostic tool for liver fibrosis in people with MASLD in both primary and secondary care. Alternative non-invasive tests or improved cut-off values are needed for accurate fibrosis detection in clinical practice.

ABSTRACT N°2

TITLE: INSIGHTS FROM THE ELPA EUROPEAN LIVER SCREENING WEEK 2024

AUTHORS

Richard Hall, European Liver Patients' Association - ELPA, Liver4Life
Jacques Schuurman, European Liver Patients' Association - ELPA, SOS Hépatites Champagne-Ardennes
Lydie Moreaux, European Liver Patients' Association - ELPA, SOS Hépatites Champagne-Ardennes
Julie Odienne, European Liver Patients' Association - ELPA, SOS Hépatites Champagne-Ardennes
Marko Korenjak, European Liver Patients' Association - ELPA, Association Slovenija Hep
Milan Mishkovikj, European Liver Patients' Association - ELPA, Hepar Centar Bitola
Veronika Vsetickova, European Liver Patients' Association - ELPA
Beatrice Credi, European Liver Patients' Association - ELPA

KEYWORDS

PREVENTION, SCREENING, FIBROSIS, NON-COMMUNICABLE DISEASES

OBJECTIVES

This project aimed to raise awareness of early liver disease detection using portable transient elastography (TE) in community settings.

METHODS

Over five days, ELPA members Liver4Life and SOS Hépatite offered TE scans to European Parliament staff and the public. Vans outside the main entrance featured targeted messaging. Trained operators, including Belgian HCPs, conducted scans. Brief lifestyle advice and referral letters were given for high CAP or stiffness readings. Participants also completed an anonymous liver health questionnaire.

RESULTS

The total number of completed and recorded examinations was 309, paired with questionnaires. These were all adults: 165 men and 144 women. Of the total examinations, 30 people (9.7%) had stiffness readings above 7.1Kpa, and these people were given self-referral letters after brief intervention advice. The highest stiffness reading over the 5 days was 12.4 Kpa. The study also identified 67 people (22%) with a CAP of 275 or higher (UK criteria) and 181 people (59%) with a CAP of 225 or higher (Belgium criteria). Everyone with a CAP of 225 or greater was given brief intervention lifestyle advice.
The average age was 44.8 years old. The average weight was 74.8 kg, height was 169.2 cm, and BMI was 26.1. 40 people had a BMI higher than 30 (9.7%).
99 people (32%) stated that they were worried their liver could be damaged, and the main reasons given were: 55 (17.7%) overweight, 50 (16.1%) thought they drank too much, and 23 (7.4%) thought they may have an auto-immune condition. There was no option to select more than a single primary reason. 38 people (12.3%) stated that they drank alcohol on 4 or more days per week, 47 people (15.2%) reported high blood pressure, and 75 people (24.2%) reported a stress level of 7 out of 10 or higher, and 77 people (24.9%) had relied on substances (alcohol, caffeine or medication) to manage their stress level.

CONCLUSIONS

This year’s larger cohort showed similar results to last year. Inconsistent criteria may lead to varied care. Many with high CAP were unaware of it, though some suspected it but avoided confirmation. The findings stress the need for public health awareness.

ABSTRACT N°3 1/2

TITLE: ROLE OF LIPID, MITOCHONDRIAL BIOENERGETICS AND SENESCENCE IN MASH USING IN VITRO CELL MODEL

AUTHORS

Bani Mukhopadhyay, NIH,NIAAA
Cheryl Marietta, NIH,NIAAA
Samantha Hoey, NIH,NIAAA
Eli Winkler, NIH,NIAAA
Keita Morisaki, NIH,NIAAA
Abdul Oiseni, VCU.Richmond.Virginia
Faridoddin Mirshahi, VCU.Richmond,Virginia
Colin Hodgkinson, NIH,NIAAA
George Kunos, NIH,NIAAA
Arun Sanyal, VCU.Richmond,Virginia
David Goldman, NIH,NIAAA

KEYWORDS

IHLCS,MITOCHONDRIA,TRANSCRIPTOME,MASH,BIOENERGETICS,

OBJECTIVES

Genetics and socio-economic status lead to risky drinking patterns and specific behavior associated with diet and health practices. These lead to the development of alcoholic steatohepatitis (ASH) or metabolic dysfunction-associated steatohepatitis (MASH).

METHODS

To understand mechanistic role, the transcriptome of hepatocyte-like cells derived from representative healthy and patients blood samples through iPSC were investigated. Healthy and MASH patient's blood samples were collected, and iPSC clones were generated from purified CD4+ T cells of their blood samples. iHLCs were generated from iPSC and were characterized. The functional assays were also performed to probe bioenergetics of the patient's derived hepatocytes. Bioenergetic profiles were determined by Seahorse mitochondrial respiratory rate using ATP rate analyses. A systemic analysis of transcriptomes of iHLCs vs patient's biopsies were performed followed by mitochondrial bioenergetics. Healthy and MASH patients' blood samples obtained from VCU and NIH were examined for a population study of various immune cells markers. Hepatocyte-like cells were generated from those healthy and patient's blood derived from iPSC cells and characterized by multiple markers.

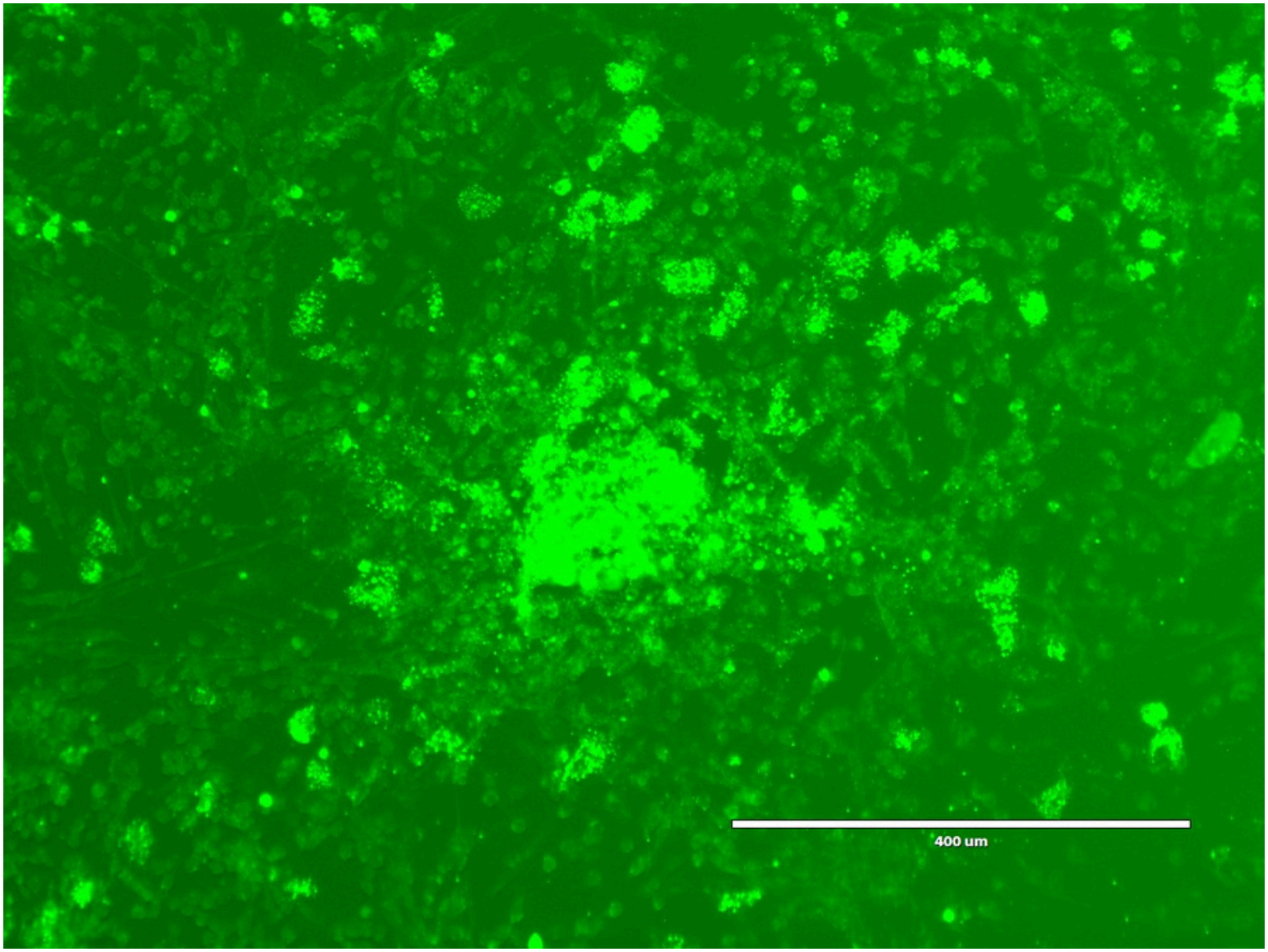
RESULTS

Hepatocyte-like cells generated from MASH patient's blood samples were observed to be like healthy samples but have distinctive characteristics of regulation of lipid, cell death pathways. The major distinctive differences are in their bioenergetic pathways with impairment of ATP production, their substrate utilization, specific set of genes for responses to lipid, cell death and senescence. MASH Patient's derived hepatocytes have distinctive transcriptome characteristics especially on metabolic pathways and impaired bioenergetic profile of MASH derived iHLCs compared to Healthy iHLCs. However, the patterns of lipid droplet and mitochondrial bioenergetics improved significantly with specific drug treatments.

CONCLUSIONS

Our patient derived cell model is significant step forward to the new NIH initiative to expand innovative, human-based science while reducing animal use in research. The functional measurement of mitochondrial oxidative phosphorylation and substrate utilization demonstrated a distinctive difference between healthy and MASH patient's derived hepatocytes. Targeting those patients-based bioenergetics and their modulation by engineering has great potential for future prospect for a precision individualized medicine of MASH patients.

ABSTRACT N°3 2/2



ABSTRACT N°4

TITLE: CORRELATION BETWEEN METABOLIC MARKERS AND LIVER STIFFNESS PROGRESSION IN PATIENTS WITH MASLD

AUTHORS

Merle Roeren, Karolinska Institutet, Stockholm, Sweden
Ying Shang, Karolinska Institutet, Stockholm, Sweden
Hannes Hagström, Karolinska Institutet, Stockholm, Sweden; Division of Hepatology, Department of Upper GI Diseases, Karolinska University Hospital, Stockholm, Sweden
The VCTE-Prognosis Consortium

KEYWORDS

MARKERS, FIBROSIS, CIRRHOSIS, ELASTOGRAPHY

OBJECTIVES

Liver stiffness measurement (LSM) by vibration-controlled transient elastography (VCTE) is used as a proxy for liver fibrosis in patients with MASLD. Guidelines for identifying patients at risk for advanced fibrosis recommend VCTE referrals based on FIB-4 thresholds. However, limited access to VCTE highlights the need for widely accessible methods to identify high-risk patients. This is especially important for patients with LSM <8kPa who are managed in primary care. Here, we aimed to assess whether changes in routinely measured markers can help prioritize patients for VCTE referral by indicating liver stiffness progression.

METHODS

The VCTE-prognosis study was a longitudinal cohort of patients with MASLD from 16 tertiary centres across the US, Europe, and Asia (2004–2023) who underwent serial assessments of routine markers and VCTE measurements. We included patients with LSM <8kPa at baseline. LSM trajectories were modelled using data-driven latent-growth mixture models to identify distinct classes of LSM progression over a 36-month period. We plotted 16 markers including lipids, glucose levels and BMI within each class to evaluate their correlation to LSM trajectories.

RESULTS

We included 10,789 patients (median age 54; 58% male). Three distinct classes of LSM trajectories were identified: Class 1 (62.4%): baseline LSM of 4.6 (95%CI: 4.5–4.6) with an annual decrease of 1.1%; Class 2 (35.8%): baseline LSM of 6.5 (95%CI: 6.5–6.5) with an annual decrease of 1.4%; Class 3 (1.8%): baseline LSM of 7.6 (95% CI: 7.2–8.1) with an annual increase of 26.7%. Among the classes, 1 (0.0%), 247 (6.4%) and 176 (88.9%) exceeded 8kPa within 3 years. Those with ≥30% LSM increase were 423 (6.3%), 328 (8.5%) and 157 (79.3%), respectively.
FIB-4 trajectories mirrored the LSM trajectories best, with an annual increase of 2.0% in Class 1, 0% in Class 2 and 15.3% in Class 3. BMI, lipids and other markers showed no correlation with LSM changes.

CONCLUSIONS

Among patients with LSM <8kPa, less than 1.8% showed increasing liver stiffness warranting further referral. Repeated FIB-4 measurements may help identify and prioritize these individuals for VCTE assessments in settings with limited access.

ABSTRACT N°5 1/2

TITLE: BARIATRIC SURGERY UNCOVERS DISSOCIATION OF METABOLIC IMPROVEMENT FROM HEPATIC OXIDATIVE CAPACITY AND HISTOLOGY

AUTHORS

Jennifer Pützer, Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research, Heinrich Heine University, Düsseldorf, Germany
Dr. Sabine Kahl, Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research, Heinrich Heine University, Düsseldorf, Germany
Dr. Cesare Granata, Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research, Heinrich Heine University, Düsseldorf, Germany
Dr. Bedair Dewidar, Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research, Heinrich Heine University, Düsseldorf, Germany
Dr. Kalliopi Pafili, Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research, Heinrich Heine University, Düsseldorf, Germany
Dr. Sandra Trenkamp, Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research, Heinrich Heine University, Düsseldorf, Germany
Prof. Irene Esposito, Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research, Heinrich Heine University, Düsseldorf, Germany
Dr. Matthias Schlensak, Adipositas- und Refluxzentrum, Krankenhaus Neuwerk, Mönchengladbach, Germany
Prof. Frank A. Granderath, Adipositas- und Refluxzentrum, Krankenhaus Neuwerk, Mönchengladbach, Germany
Prof. Michael Roden, Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research, Heinrich Heine University, Düsseldorf, Germany

KEYWORDS

MASLD, MITOCHONDRIAL-RESPIRATION, BARIATRIC-SURGERY, INSULIN-SENSITIVITY, LIVER

OBJECTIVES

Hepatic mitochondrial oxidative phosphorylation (OXPHOS) capacity fails to adapt during the progression of MASLD (metabolic dysfunction-associated steatotic liver disease). We aimed to investigate whether improved insulin sensitivity after bariatric surgery is also associated with hepatic OXPHOS changes in individuals with class III obesity, with or without MASLD.

METHODS

Sixteen individuals (BMI 53±8 kg/m²) underwent liver biopsies during bariatric surgery and again during elective follow-up surgery (median follow-up: 24 months). Whole-body insulin sensitivity (M-value) was assessed using hyperinsulinemic-euglycemic clamps. Adipose tissue insulin resistance from the Adipo-IR was calculated as the product of fasting insulin and fasting non-esterified fatty acids. Maximum coupled hepatic OXPHOS capacity was measured by high-resolution respirometry and mitochondrial DNA (mtDNA) content was quantified by qRT-PCR. MASLD staging was based on liver histology. Paired comparisons between baseline and follow-up values were assessed using the Wilcoxon signed-rank test.

RESULTS

Following surgery, participants experienced a 33% reduction in body weight (from 151.7±21.0 kg to 102.7±12.0 kg; p<0.0001). Adipose tissue insulin resistance (Adipo-IR) decreased by 59% (p=0.004), while mean M-value changed from 3.58 to 5.73 mg/kg/min (p=0.055, n=8). Although liver lipid content decreased in all participants from 25.4% to 2.9% (p=0.0002), lobular inflammation and ballooning showed inconsistent changes. Hepatic OXPHOS capacity remained unchanged either corrected for wet weight or for mtDNA content. No associations were found between the individual changes in hepatic OXPHOS capacity and insulin sensitivity or liver histology.

ABSTRACT N°5 2/2

CONCLUSIONS

Bariatric surgery profoundly reduces hepatic steatosis and adipose tissue insulin resistance, but does not necessarily affect hepatic OXPHOS capacity and histology. These findings suggest a dissociation between systemic metabolic alterations and both hepatic oxidative function and inflammation underlining the need for mitochondria-targeted therapies in MASLD.

ABSTRACT N°6 1/2

TITLE: DEVELOPMENT AND VALIDATION OF TWO NIS2+®-BASED MODELS TO DETECT MASH RESOLUTION AND FIBROSIS IMPROVEMENT

AUTHORS

MD VLAD RATZIU, Sorbonne Université, Institute for Cardiometabolism and Nutrition, Hôpital Pitié-Salpêtrière, Paris, France
MD SVEN FRANCQUE, Gastroenterology and Hepatology, Antwerp University Hospital, Antwerp, Belgium
MSc YACINE HAJJI, Genfit S.A., Loos, France
PhD JEREMY MAGNANENSI, Genfit S.A., Loos, France
PhD ZOUHER MAJD, Genfit S.A., Loos, France
PhD DEAN HUM, Genfit S.A., Loos, France
PhD BART STAELS, Université de Lille, INSERM, CHU Lille, Institut Pasteur de Lille U1011, Lille, France
FRCP, PhD QUENTIN ANSTEE, Translational and Clinical Research Institute, Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, UK
MD ARUN SANYAL, Division of Gastroenterology, Hepatology and Nutrition, Virginia Commonwealth University School of Medicine, Richmond, Virginia, USA

KEYWORDS

NIS2+®, MONITORING, MASH-RESOLUTION, FIBROSIS IMPROVEMENT

OBJECTIVES

The approval of Rezdiffra™ to treat patients with MASH and fibrosis 2-3 further increases the need for an efficient non-invasive monitoring tool to identify patients who meet the histological endpoints of MASH clinical trials (MASH resolution [EP1], fibrosis improvement [EP2]). NIS2+® is a blood-based biomarker developed for at-risk MASH (MAS≥4; F≥2) detection. We aimed to develop and validate predictive models for EP1 and EP2 based on demographic data and successive NIS2+® measurements.

METHODS

Patients included in the RESOLVE-IT phase 3 trial (NCT02704403) with MASH, MAS≥4, fibrosis 1-3 at baseline, and NIS2+® available at all 8 trial visits were selected (N=703). This cohort was randomly split in training (N=280, 40%) and test (N=423, 60%) sets. Using logistic Lasso regression, demographic features and features describing NIS2+® changes over time were selected in the training set to build two models (M1 for EP1, M2 for EP2). For each model, low (Lc) and high (Hc) cutoffs were derived to respectively reach a sensitivity and specificity of 0.80. Performance of M1 and M2 were validated in the test set and evaluated for decreasing number of NIS2+® measures collected between baseline and end-of-study visits.

RESULTS

Mean follow-up was 19 months. Prevalences of EP1 and EP2 ranged 21%-23% in both training and test sets. In test set, M1 reached an AUC of 0.81 for the detection of EP1. At Lc (0.41), M1 exhibited a sensitivity of 0.80, specificity of 0.67 and NPV of 0.93, while at Hc (0.52), specificity was 0.79, sensitivity 0.68 and PPV 0.46. M2 achieved an AUC of 0.74 for the detection of EP2. At Lc (0.48), M2 showed a sensitivity of 0.72, specificity of 0.61 and NPV of 0.88, while at Hc (0.56), specificity was 0.78, sensitivity 0.53 and PPV 0.41. Similar AUCs were observed when using only 4 NIS2+® measures during follow-up vs 8 (M1: 0.80 vs 0.81, p=0.54; M2: 0.74 vs 0.74, p=0.68).

CONCLUSIONS

We developed and validated two NIS2+®-based models with high performance in ruling-in/out MASH resolution and fibrosis improvement. Models with four NIS2+® measurements over approximately 1.5 years using Hc allow for potential application in monitoring treatment response.

ABSTRACT N°6 1/2

	MASH resolution model		Fibrosis improvement model	
	Training set (N=280)	Test set (N=423)	Training set (N=280)	Test set (N=423)
Prevalence	0.23 (64)	0.21 (88)	0.23 (65)	0.22 (94)
AUC	0.850 (0.798-0.902)	0.811 (0.760-0.862)	0.777 (0.714-0.839)	0.741 (0.687-0.796)
Rule-in cutoff (80% specificity)	0.52		0.56	
Accuracy	0.79 (0.74-0.83)	0.77 (0.72-0.81)	0.74 (0.68-0.79)	0.73 (0.68-0.77)
Sensitivity	0.75 (0.62-0.85)	0.68 (0.57-0.77)	0.52 (0.40-0.65)	0.53 (0.43-0.63)
Specificity	**0.80** (0.74-0.85)	0.79 (0.74-0.83)	**0.80** (0.74-0.85)	0.78 (0.73-0.82)
PPV	0.53 (0.42-0.63)	0.46 (0.37-0.55)	0.44 (0.33-0.56)	0.41 (0.32-0.50)
IRZ	0.14 (39)	0.12 (52)	0.19 (54)	0.18 (75)
Rule-out cutoff (80% sensitivity)	0.41		0.48	
Accuracy	0.69 (0.63-0.74)	0.69 (0.65-0.74)	0.67 (0.61-0.73)	0.63 (0.59-0.68)
Sensitivity	**0.83** (0.71-0.91)	0.80 (0.69-0.87)	**0.80** (0.68-0.89)	0.72 (0.62-0.81)
Specificity	0.64 (0.58-0.71)	0.67 (0.61-0.72)	0.63 (0.56-0.70)	0.61 (0.55-0.66)
NPV	0.93 (0.87-0.96)	0.93 (0.88-0.95)	0.91 (0.85-0.95)	0.88 (0.83-0.92)

ABSTRACT N°7 1/2

TITLE: DEVELOPMENT OF A MACHINE LEARNING MODEL FOR PREDICTING SIGNIFICANT FIBROSIS IN SEVERELY OBESE MASH PATIENTS

AUTHORS

Ahmed Cordie, Cairo University Hospitals, Endemic hepatogastroenterology and infectious diseases department, Cairo, Egypt.
Rabab Omar, Cairo University Hospitals, Endemic hepatogastroenterology and infectious diseases department, Cairo, Egypt.
Eissa Abdeaal, Cairo University Hospitals, Endemic hepatogastroenterology and infectious diseases department, Cairo, Egypt.
Mohamed Fahmy, Cairo University Hospitals, General and Laparoscopic surgery, Cairo, Egypt.
Dina Helmy, Department of Pathology, Faculty of Medicine, Cairo University, Cairo, Egypt.
Sherif Musa, Cairo University Hospitals, Endemic hepatogastroenterology and infectious diseases department, Cairo, Egypt.
Heba Omar, Cairo University Hospitals, Endemic hepatogastroenterology and infectious diseases department, Cairo, Egypt.
Ahmed Kamel, Department of Clinical Pharmacy, Faculty of Pharmacy, Cairo University, Cairo, Egypt.
Abdullah Elhakim, Cairo University Hospitals, Endemic hepatogastroenterology and infectious diseases department, Cairo, Egypt.

KEYWORDS

NON-INASIVE, OBESE, MASH, FIBROSIS, BIOMARKERS

OBJECTIVES

Current non-invasive tests (NITs) for liver fibrosis demonstrate suboptimal performance in patients with severe obesity and metabolic dysfunction-associated steatohepatitis (MASH). Traditional biomarker thresholds derived from mixed populations are fundamentally misaligned with the metabolic complexity of severe obesity, leading to high rates of missed diagnoses and delayed treatment initiation. We developed a novel machine learning model specifically optimized for predicting significant fibrosis (F≥2) in this high-risk population.

METHODS

This study included patients with severe obesity (BMI ≥40 kg/m²) and biopsy-confirmed fibrosis staging. We evaluated established NITs (APRI, FIB-4, MAF-5, NFS, FAST, AGILE 3+) using published thresholds and developed a Random Forest classifier using routine clinical parameters. Feature selection employed Random Forest-based importance ranking from 18 variables, identifying age, BMI, AST/ALT (normalized to ULN), platelet count, HbA1c, liver stiffness measurement (LSM), and controlled attenuation parameter (CAP) as key predictors. Model development used a 70/30 train-test split with 10-fold cross-validation. Performance was compared against established NITs using identical test samples.

RESULTS

The cohort comprised 95 patients (86.3% females, mean age 40.4 years, median BMI 43.3 kg/m², and diabetes prevalence of 28.4%). Biopsy results showed 28.4% with no fibrosis (F0), 37.9% with F1, 23.2% with F2, and 10.5% with F3, yielding a 33.7% significant fibrosis (F≥2) prevalence. Established NITs demonstrated suboptimal performance at published thresholds: rule-out sensitivity from 6% (MAF-5) to 62% (FAST), while rule-in sensitivity was 0-19% for most scores. The Random Forest model achieved cross-validation AUC of 0.86 and test AUC of 0.80, with 83% sensitivity and 92% specificity. Test performance exceeded all established NITs: FAST (AUC 0.74), AGILE 3+ (AUC 0.74), MAF-5 (AUC 0.77), FIB-4 (AUC 0.61), and others (AUC 0.59-0.72). The model maintained consistent performance using elastography-derived parameters (CAP, LSM) alongside routine laboratory values, achieving superior accuracy compared to established scores using similar elastography components.

CONCLUSIONS

We developed a novel machine learning model that significantly outperforms established NITs for fibrosis detection in severe obesity MASH patients. The model's superior accuracy using both routine clinical parameters and elastography measurements provides enhanced diagnostic utility. This addresses critical gaps in current diagnostic tools, supporting improved risk stratification in this challenging patient population.

ABSTRACT N°7 2/2

Table 1: Model Performance Comparison

Model	CV AUC	Test AUC	Sensitivity	Specificity	N
ML Random Forest	**0.86**	**0.80**	**0.83**	**0.92**	**19**
SAFE	0.66	0.77	0.67	0.85	19
ML XGBoost	0.71	0.80	0.83	0.85	19
ML Elastic Net	0.81	0.78	0.83	0.85	19
FAST	0.73	0.74	0.83	0.75	18
AGILE 3+	0.68	0.74	1.00	0.50	18
APRI	0.67	0.72	0.67	0.85	19
NFS	0.65	0.68	1.00	0.46	19
FIB-4	0.66	0.61	0.33	1.00	19
BARD	0.61	0.61	0.50	0.77	19
HFS	0.59	0.59	0.50	0.77	19
LSM (KPA)	0.77	0.59	0.33	0.92	19

Table 2: Established NITs Performance at Literature Thresholds

Score	Rule-Out Threshold	Sensitivity	Specificity	Rule-In Threshold	Sensitivity	Specificity
APRI	0.50	0.28	0.90	1.50	0.03	1.00
FIB-4	1.45	0.19	0.94	3.25	0.03	1.00
MAF-5	-0.50	0.06	0.98	1.00	0.00	1.00
NFS	-1.46	0.91	0.41	0.68	0.19	0.92
SAFE	-0.50	0.00	1.00	1.00	0.00	1.00
HFS	0.12	0.00	1.00	0.47	0.00	1.00
BARD	1.00	1.00	0.00	2.00	0.88	0.22
FAST	0.35	0.62	0.77	0.67	0.12	0.95
AGILE 3+	0.45	0.31	0.90	0.68	0.09	0.98

ABSTRACT N°8

TITLE: PREVALENCE OF MASLD AND ADVANCED FIBROSIS IN MIDDLE-AGED ADULTS: INSIGHTS FROM THE SWEDISH SCAPIS COHORT

AUTHORS

Dr Oumarou Nabi, Department of Medicine, Huddinge, Karolinska Institutet, Stockholm, Sweden
Dr Jonas Spaak, Department of Medicine, Huddinge, Karolinska Institutet, Stockholm, Sweden
Dr Daniel P. Andersson, Department of Medicine, Huddinge, Karolinska Institutet, Stockholm, Sweden
Dr Hannes Hagström, Department of Medicine, Huddinge, Karolinska Institutet, Stockholm, Sweden

KEYWORDS

PREVALENCE, MASLD, LIVER FIBROSIS

OBJECTIVES

Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common chronic liver disease globally, yet its prevalence and severity remain poorly characterized in general populations. We aimed to estimate the prevalence of MASLD and risk for advanced fibrosis in a large Swedish cohort.

METHODS

We analyzed 27,763 participants from the SCAPIS cohort who underwent extensive clinical characterization. MASLD was defined as <48 Hounsfield Units on non-contrast liver CT imaging. The risk for advanced fibrosis was assessed using the dynamic AST/ALT ratio.

RESULTS

MASLD was present in 18.1% of participants and was more common in men than women (25.5% vs. 11.2%). Prevalence increased with cardiometabolic burden: from 6.2% among those without obesity, hypertension, or T2DM to 63.6% among those with all three conditions. MASLD risk was elevated in individuals with obesity alone (adjusted odds ratio [aOR] 5.85; 95% CI: 5.10-6.71), T2DM alone (aOR 2.11; 95% CI: 1.79-2.47), or hypertension alone (aOR 1.97; 95% CI: 1.75-2.22). The combination of all three conferred the highest risk (aOR 12.30; 95% CI: 10.30-14.50). Among MASLD cases, 24.8% were classified as at risk for advanced fibrosis. Fibrosis risk was independently associated with hypertension (aOR 1.45; 95% CI: 1.26-1.67), T2DM (aOR 1.27; 95% CI: 1.10-1.46), and male sex (aOR 1.30; 95% CI: 1.12-1.51).

CONCLUSIONS

MASLD affects nearly one in five middle-aged adults in Sweden, with a quarter of cases at risk for advanced fibrosis. Obesity, T2DM, and hypertension are key predictors of MASLD prevalence and severity.

ABSTRACT N°9 1/2

TITLE: ENDOTHELIAL-TO-MESENCHYMAL TRANSITION IN MASLD-ASSOCIATED LIVER CARCINOGENESIS

AUTHORS

Ms Victoria Priori, Université Paris-Cité, INSERM 1149, Centre de Recherche sur l'Inflammation, F-75018 Paris, France
Ms Camille Pignolet, Université Paris-Cité, INSERM 1149, Centre de Recherche sur l'Inflammation, F-75018 Paris, France
Dr Samira Laouirem, Université Paris-Cité, INSERM 1149, Centre de Recherche sur l'Inflammation, F-75018 Paris, France
Dr Alexandre Sayadi, Université Paris-Cité, INSERM 1149, Centre de Recherche sur l'Inflammation, F-75018 Paris, France. Département de Pathologie, Hôpital Beaujon, Assistance Publique-Hôpitaux de Paris, Clichy, France
Dr Etienne Becht, Université Paris-Cité, INSERM 1149, Centre de Recherche sur l'Inflammation, F-75018 Paris, France
Dr Aurélie Beaufrère, Université Paris-Cité, INSERM 1149, Centre de Recherche sur l'Inflammation, F-75018 Paris, France. Département de Pathologie, Hôpital Beaujon, Assistance Publique-Hôpitaux de Paris, Clichy, France
Dr Rémy Nicolle, Université Paris-Cité, INSERM 1149, Centre de Recherche sur l'Inflammation, F-75018 Paris, France
Dr Adel Hammoutene, Université Paris-Cité, INSERM 1149, Centre de Recherche sur l'Inflammation, F-75018 Paris, France
Prof Valérie Paradis, Université Paris-Cité, INSERM 1149, Centre de Recherche sur l'Inflammation, F-75018 Paris, France. Département de Pathologie, Hôpital Beaujon, Assistance Publique-Hôpitaux de Paris, Clichy, France

KEYWORDS

ENDOTHELIAL-TO-MESENCHYMAL-TRANSITION, HCC, ENDOTHELIAL, MASLD, SINGLE-CELL-RNA-SEQUENCING

OBJECTIVES

MASLD is becoming the main risk for hepatocellular carcinoma (HCC). HCC is a highly vascularized tumor in which endothelial cells play a critical role in its initiation and progression, including in MASLD. Endothelial-to-mesenchymal transition (EndMT) is the process by which endothelial cells progressively lose their specific characteristics and acquire mesenchymal properties. While this phenomenon is extensively studied in cardiovascular and pulmonary diseases, it remains poorly explored in chronic liver disease and HCC. In this study, we aimed to investigate the dynamics of EndMT and decipher its potential contribution in MASLD-related HCC.

METHODS

Primary human liver endothelial cells (LECs) were immunomagnetically [CD146+] isolated from fresh liver tissue of MASLD patients, with varying stages of steatosis, activity and fibrosis. Single-cell suspensions of LECs from HCC (n=5) and non-tumoral liver (n=14) were processed for single-cell RNA sequencing (scRNA-seq). In addition to a standard clustering process, independent component analysis (ICA) was applied to the transcriptomic data to identify sub-phenotypes and their associated genes, defined by the top-contributing genes of each independent component. The identified signatures were subsequently projected onto independent open-access public scRNA-seq datasets to validate LECs subpopulations.

RESULTS

scRNA-seq identified 10 clusters, sorted into 4 distinct LEC populations organized along a differentiation continuum from liver sinusoidal endothelial cells (LSECs) to fibroblastic phenotypes. Based on gene expression profiling, these groups of population corresponded to 1-healthy LSECs (LSECs, with neither capillarization nor EndMT, expressing STAB-2, LYVE-1), 2-capillarized LSECs (expressing VWF, PECAM1), 3-LECs undergoing EndMT (STAB-2, LYVE-1 downregulated and expressing FN1, VIM), and 4-LECs with mesenchymal phenotype (expressing ACTA2, PDGFR-β). Transitional LECs were enriched in cirrhotic and HCC samples. Mesenchymal cells were mainly tumor-associated LECs, suggesting a potential involvement of EndMT in HCC progression. Neither steatosis nor activity levels significantly impacted EndMT profile.

CONCLUSIONS

By illustrating the high plasticity of human LECs, this study supports the central role of LECs in HCC and highlights that EndMT occurs during MASLD-related liver carcinogenesis. By categorizing LECs into distinct subpopulations, we were able to pinpoint stage-specific markers of the EndMT process. Further analyses will determine whether EndMT could be reversed and targeted as a therapeutic strategy for HCC.

ABSTRACT N°9 2/2

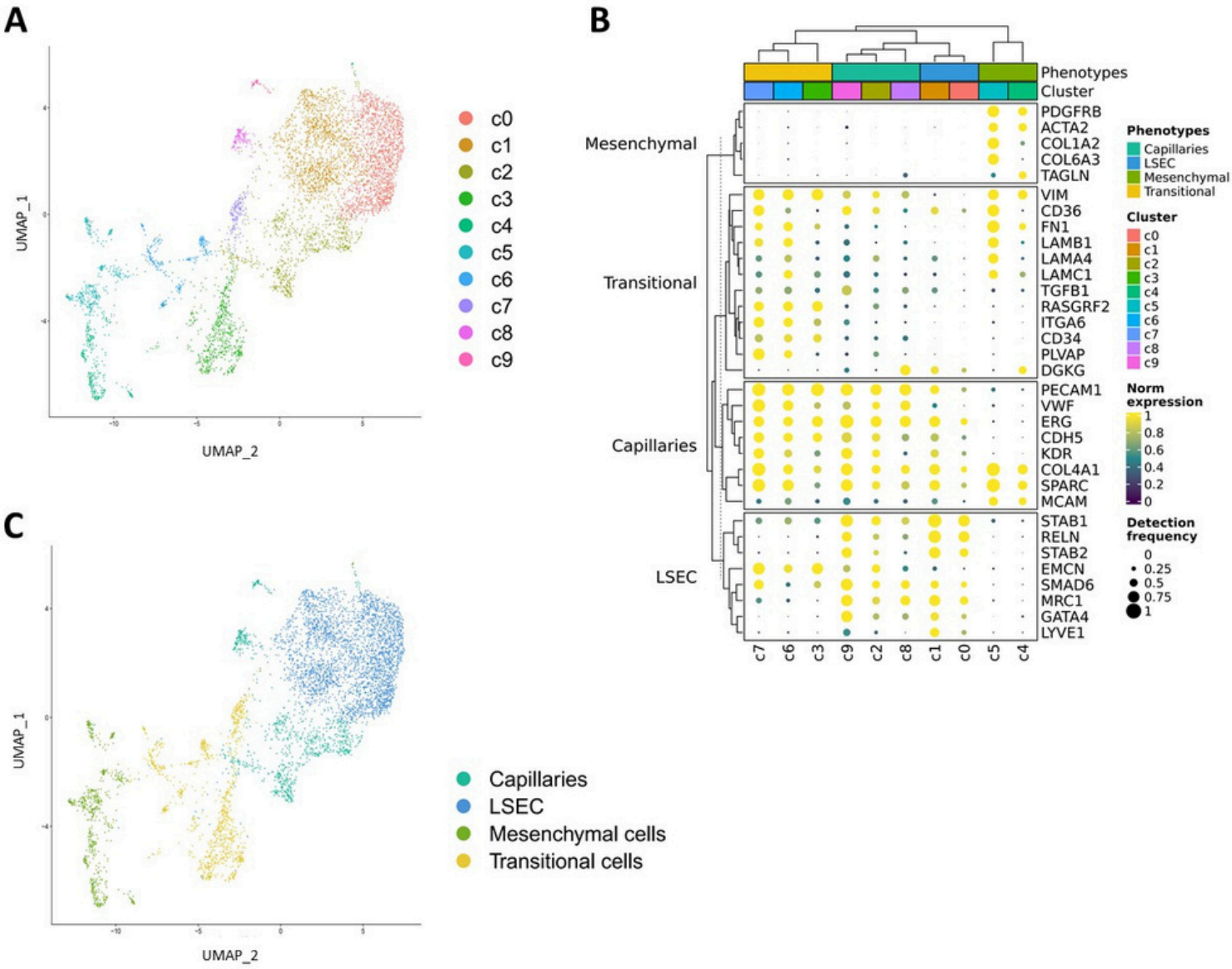


Figure. Single-cell RNA-seq analysis of human MASLD-liver endothelial cells (LECs) from non tumoral and HCC samples. (A) UMAP of endothelial cells (n=5 HCC, n=14 NTL) after exclusion of non-endothelial populations (resolution = 0.3). **(B)** Dot plot showing key marker gene expression across clusters, grouped by cell type. **(C)** UMAP identifying four endothelial subtypes: LSEC, capillaries, transitional, and mesenchymal cells.

Abbreviations: HCC: Hepatocellular carcinoma; LSEC: Liver sinusoidal endothelial cell; NTL: Non tumoral Liver; UMAP: Uniform Manifold Approximation and Projection.

ABSTRACT N°10 1/2

TITLE: DYNAMICS OF NON-INVASIVE OF TESTS IN PATIENTS WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

AUTHORS

Hannes Hegmar, Department of Medicine, Huddinge, Karolinska Institutet, Stockholm, Sweden
Rickard Strandberg, Department of Medicine, Huddinge, Karolinska Institutet, Stockholm, Sweden
Ying Shang, Department of Medicine, Huddinge, Karolinska Institutet, Stockholm, Sweden
Johan Vessby, Department of Medical Sciences, Gastroenterology Research Group, Uppsala University, Uppsala, Sweden
Åsa Danielsson Borsén, Umeå University Hospital, Umeå, Sweden
Nils Nyhlin, Department of Gastroenterology, Faculty of Medicine and Health, Örebro University, Örebro, Sweden
Stergios Kechagias, Department of Gastroenterology and Hepatology, Department of Health, Medicine and Caring Sciences, Linköping University, Linköping, Sweden
Per Stål, Department of Medicine, Huddinge, Karolinska Institutet, Stockholm, Sweden
SWEHEP study group
Mattias Ekstedt, Department of Gastroenterology and Hepatology, Department of Health, Medicine and Caring Sciences, Linköping University, Linköping, Sweden
Hannes Hagström, Department of Medicine, Huddinge, Karolinska Institutet, Stockholm, Sweden

KEYWORDS

MASLD, FIBROSIS, NON-INVASIVE TESTS, LIVER-STIFFNESS

OBJECTIVES

Non-invasive tests (NIT) are frequently used for monitoring of patients with metabolic dysfunction-associated steatotic liver disease (MASLD). NITs are also used to guide initiation of pharmacological treatment and monitor treatment response. This study examined longitudinal changes of NITs in MASLD.

METHODS

This was a prospective cohort study of patients with MASLD included between 2016-2022 from seven Swedish university hospitals. Patients (n=252) were followed for three years, with visits at baseline, one year, and three years. Clinical data, medications, routine laboratory tests, and liver stiffness measurement (LSM) by vibration-controlled transient elastography (VCTE) was performed at each visit. The NITs evaluated included LSM, FIB-4, and CAP.

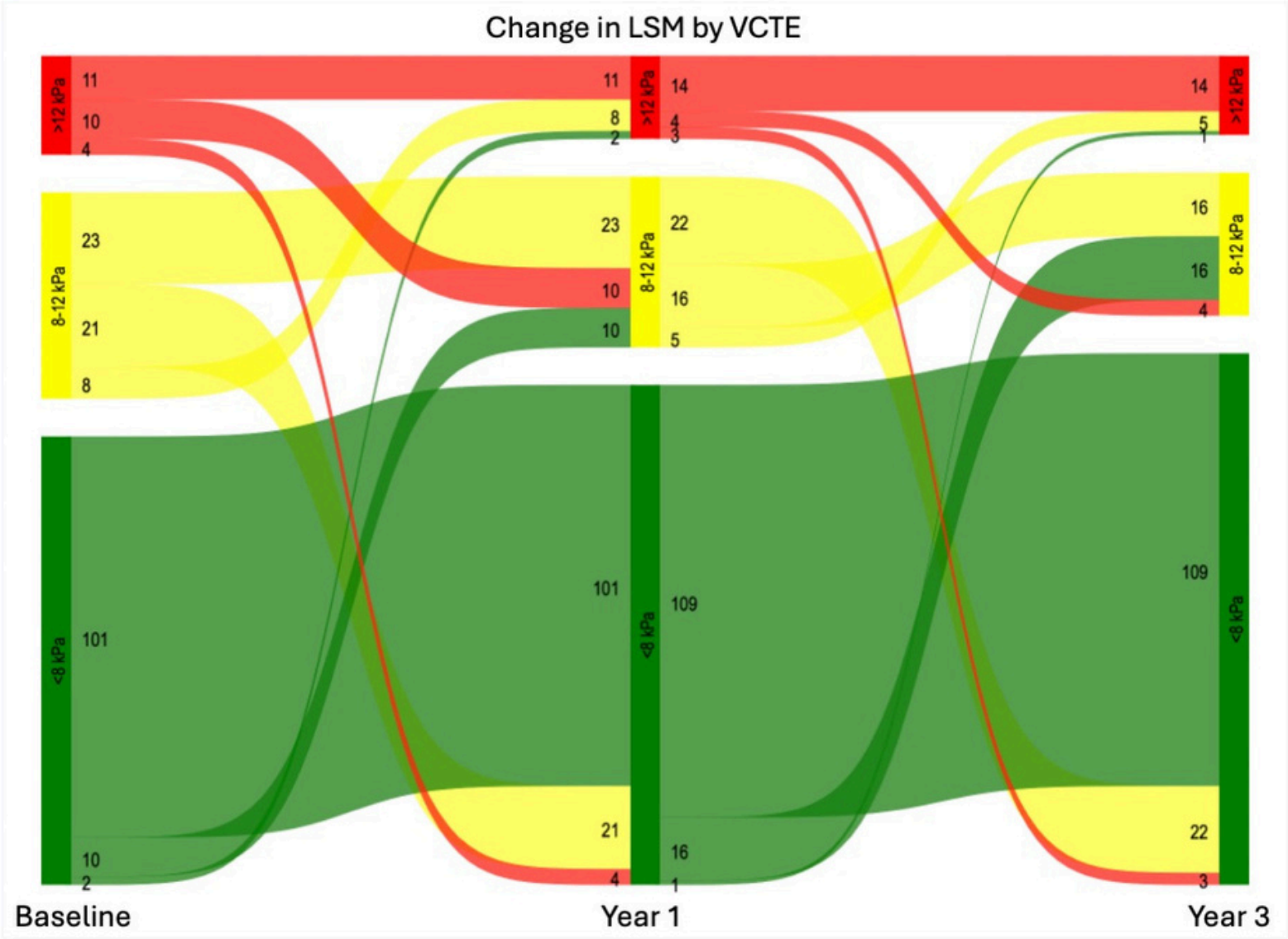
RESULTS

A total of 190 patients had a reliable LSM at all visits. The mean change in LSM was -0.13 kPa per year (95% confidence interval=-0.39 to +0.13). In patients with a baseline LSM between 8-12 kPa (n=52/190 (27%)), 56% (n=29) changed LSM category at year one (to <8 kPa or >12 kPa). In patients with an LSM between 8-12 kPa at year one, 63% (n=27) changed LSM category until year three. FIB-4 (n=233) increased by a mean 0.04 per year (95%CI=0.01-0.06). In patients with a baseline FIB-4 of 1.3-2.67 (n=87/233 (37%), 22% (n=19) changed FIB-4 category between baseline and year one. In patients with a FIB-4 of 1.3-2.67 at year one, 26% (n=24) changed FIB-4 category between year one and three.

CONCLUSIONS

On a group level, mean changes in NITs over a three-year period in MASLD were negligible. However, substantial intraindividual fluctuations was observed, highlighting the limitations of these biomarkers in reliably monitor disease progression and possibly therapeutic response.

ABSTRACT N°10 2/2



ABSTRACT N°11

TITLE: RISK OF LIVER CIRRHOSIS ACROSS OCCUPATIONAL GROUPS IN SWEDEN: A REGISTER-BASED CASE-CONTROL STUDY

AUTHORS

Marie Zalesiak, Department of Medicine, Huddinge, Karolinska Institutet, Stockholm, Sweden
Dr. Juan Vaz, Department of Medicine, Huddinge, Karolinska Institutet, Stockholm, Sweden; School of Public Health and Community Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden
Dr. Eralda Asllanaj, Center of Excellence Real World Evidence, Boehringer Ingelheim, Amsterdam, Netherlands
Dr. Martin Henriksson, Centre for Medical Technology Assessment, Department of Medical, Health and Caring Sciences, Linköping University, Linköping, Sweden
Dr. Hannes Hagström, Department of Medicine, Huddinge, Karolinska Institutet, Stockholm, Sweden; Unit of Hepatology, Department of Upper GI Diseases, Karolinska University Hospital, Stockholm, Sweden
Dr. Ying Shang, Department of Medicine, Huddinge, Karolinska Institutet, Stockholm, Sweden

KEYWORDS

LIVER CIRRHOSIS; OCCUPATION; SOCIOECONOMIC FACTORS

OBJECTIVES

The workplace serves as a valuable opportunity for targeted public health prevention. Our objective was to identify occupational groups with elevated risk of liver cirrhosis, stratified by underlying etiologies, and provide actionable evidence for targeted health promotion and early detection strategies within high-risk occupation categories.

METHODS

We conducted a nationwide case-control study using comprehensive Swedish national registry data. Identified cases were individuals aged 35–65 and diagnosed with liver cirrhosis from January 1, 2002, to December 31, 2021. We matched each case with up to four controls by age, sex, year of diagnosis, and municipality of residence. Occupational data at the index date (date of diagnosis) was sourced from the Longitudinal Integration Database for Health Insurance and Labor Market Studies, using the 30 most frequent occupational groups that represent 47% of employees in Sweden. Also, we identified information on unemployment at the index date and missing occupation. The adjusted odds ratio (aOR) was estimated using conditional logistic regression, which accounted for socioeconomic indicators (income level, education, country of birth), with Physical and Engineering Science Professionals as the reference occupation, considered a homogeneous group at low risk for liver cirrhosis.

RESULTS

The study included 23,038 cases and 92,125 matched controls. Cases disproportionately belonged to lower socioeconomic strata, as reflected by lower income, lower education, and higher unemployment rates. Service occupations exhibited significantly increased odds, ranging from aOR of 2.00 (95% CI 1.53–2.61) for childminders/teaching assistants to 2.96 (95% CI 2.25–3.90) for food preparation assistants. Manual labor occupations also had elevated risks, notably refuse collectors (aOR 3.50, 95% CI 2.73–4.48) and paper and pulp plant operators (aOR 1.90, 95% CI 1.42–2.53). Unemployment at the index date was associated with the highest odds of liver cirrhosis (aOR 4.48; 95% CI, 3.59–5.60). Stratified analyses by underlying etiology (alcohol-related liver disease and chronic viral hepatitis) demonstrated similar occupational risk patterns.

CONCLUSIONS

We identified specific occupational groups with significantly elevated odds of liver cirrhosis. While not implying causation, these findings highlight opportunities for targeted screening and intervention programs in collaboration with occupational health services and labor unions.

ABSTRACT N°12 1/2

TITLE: SPATIAL STUDY BY MULTIPLEX IMMUNOFLUORESCENCE OF HEPATOCELLULAR CARCINOMA'S IMMUNE INFILTRATION IN MASLD CONTEXT

AUTHORS

Margaux Delaporte, University Rennes, INSERM, EHESP, Irset - UMR_S 1085, 9 2 Avenue du Professeur Léon Bernard, 35000 Rennes, France.
Maëlle Guillout, University Rennes, CNRS, Inserm, Biosit UAR 3480 US_S 018, France-BioImaging (ANR-24-INBS-0005 FBI BIOGEN), Core Facility H2P2, 35000 Rennes, France.
Nicolas Gallez, University Rennes, INSERM, EHESP, Irset - UMR_S 1085, 9 2 Avenue du Professeur Léon Bernard, 35000 Rennes, France.
Anthony Sébillot, University Rennes, CNRS, Inserm, Biosit UAR 3480 US_S 018, France-BioImaging (ANR-24-INBS-0005 FBI BIOGEN), Core Facility H2P2, 35000 Rennes, France.
Orlando Musso, University Rennes, INRAE, INSERM, NUMECAN - UMR_S 1241 & Department of Pathology, CHU, 2 Rue Henri le Guilloux, 35000 Rennes, France
Michel Samson, University Rennes, INSERM, EHESP, Irset - UMR_S 1085, 9 2 Avenue du Professeur Léon Bernard, 35000 Rennes, France.
Céline Raguénès-Nicol, University Rennes, INSERM, EHESP, Irset - UMR_S 1085, 9 2 Avenue du Professeur Léon Bernard, 35000 Rennes, France.

KEYWORDS

MULTIPLEX IMAGING, TUMOR IMMUNE MICROENVIRONMENT

OBJECTIVES

MASLD is the most common chronic liver disease, with rising prevalence in Western countries. It can progress to hepatocellular carcinoma (HCC), the third leading cause of cancer-related death globally. Immune cells play a key role in HCC development, but the immune environment is highly variable, affecting targeted therapies responses. Understanding the tumour microenvironment according to the aetiology is essential. In MASLD-related HCC, we aim to assess whether alcohol consumption alters the immune state, potentially requiring different therapeutic approaches.

METHODS

We developed a multiplex immunofluorescence panel (CellDIVE™) to detect 24 markers on a single FFPE tissue section, using iterative labelling and fluorochrome inactivation. This panel is applied to HCC biopsies from patients with MASLD, stratified by alcohol use. Quantitative analysis and cell identification were performed with QuPath, using a trained model for tissue segmentation, region annotation, and automated cell subtype classification across all samples.

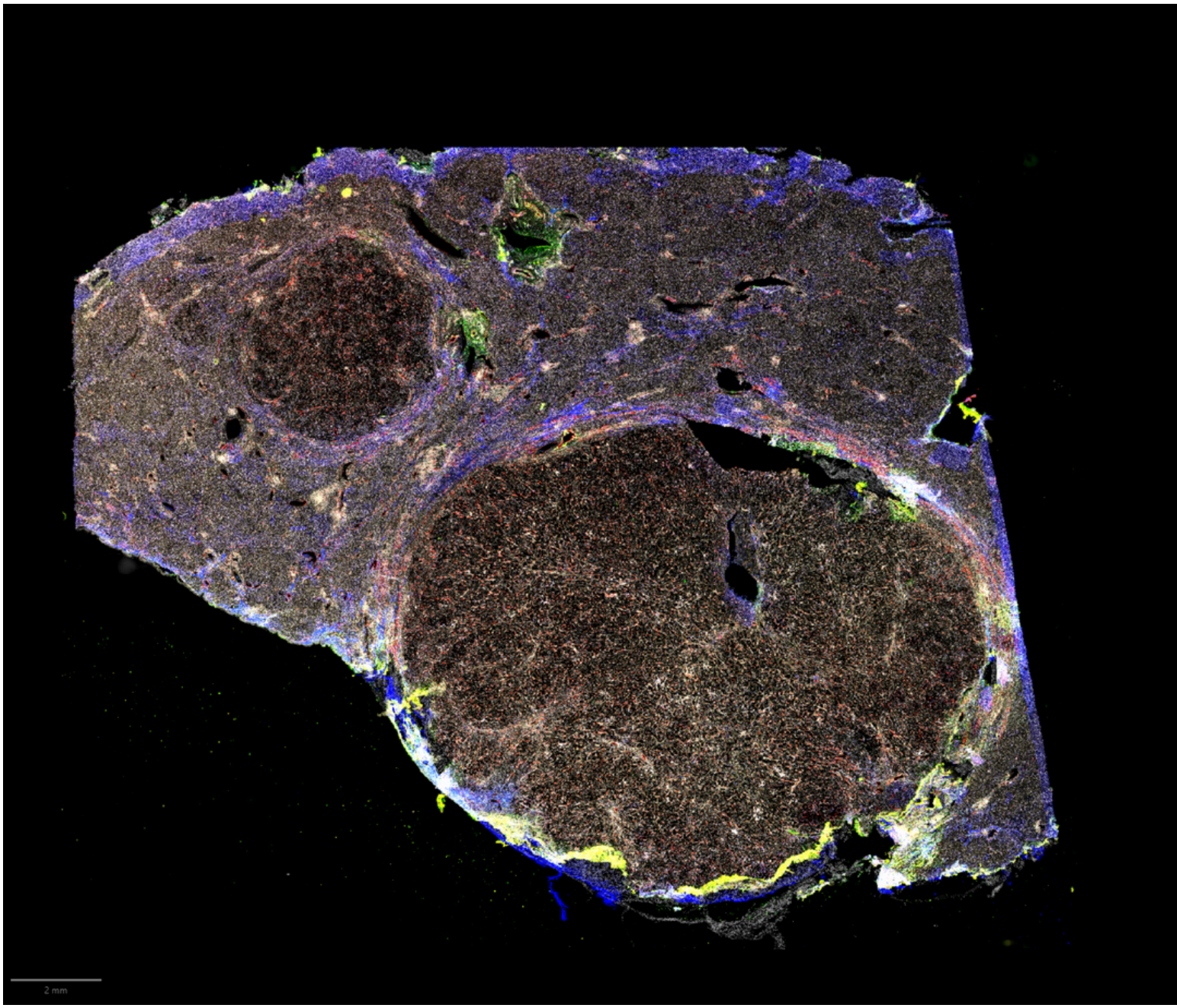
RESULTS

Using CellDIVE™, we imaged single tissue sections from 43 patients, applying 24 markers covering cell positioning, structural markers of normal or pathological liver, vascular markers, markers of myeloid and general lymphoid populations. We have integrated markers of T lymphocyte subpopulations, activation and depletion markers and immune checkpoints. Tumour and non-tumour areas were analyzed. After machine-learning-based segmentation and classification, we present preliminary findings on immune infiltrates in this cohort.

CONCLUSIONS

This multiplex imaging panel, validated on human liver, enables us to carry out a detailed mapping of the immune infiltrate of each biopsy studied. Analysis of these images will enable us to quantify the presence and location of immune cells according to patients' alcohol consumption, and may help determine whether an immunotherapy is more likely to work on certain groups, thereby helping to improve the range of treatments available. The panel is also adaptable for the study of immune infiltration to other liver diseases and non-liver tissues.

ABSTRACT N°12 1/2



ABSTRACT N°13 1/2

TITLE: PHASE 2 CLINICAL PROTOCOL EVALUATING EFFICACY AND SAFETY OF NA-941 IN ADULT PATIENTS WITH MASH

AUTHORS
Dr. Lloyd Tran, Biomed Industries, Inc
Ms. Fern Vu, Biomed Industries, Inc
Dr. Zung Tran, Biomed Industries, Inc

KEYWORDS
NA-941, MASH, BIOMED, IGF-1, NA-931

OBJECTIVES
NA-941 is a metabolite of IGF-1, which may reduce steatosis by suppressing de novo lipogenesis and increasing β oxidation. IGF-1 may prevent fibrosis by suppressing hepatic stellate cell activation. NA-941 regulates the homeostasis of quadruple functions agonists: IGF-1, GLP-1 and GIP and Glucagon receptors.
NA-941 has shown a proof of safety and efficacy in Phase 1B clinical trials.
NA-941 is an analog of NA-931 which has shown a proof of safety and efficacy in Phase 2 for the treatment of obesity.
The following is a summary of the Phase 2 clinical protocol to evaluate the efficacy and safety of NA-941 in adult patients with MASH.

METHODS
Approximately 180 patients who are eligible for participation in the study will be randomized on Day 1 in a 2:1 ratio to 50 mg NA-941 or placebo daily orally, for 48 weeks of treatment.

Key Inclusion Criteria:
Histological diagnosis of MASH with NAS ≥ 4 and NASH-CRN fibrosis score of 2 or 3 based on the consensus method of histological assessment. A historical liver biopsy within 6 months of Screening with reading confirmed during the Screening period by a consensus panel is acceptable.
AST > 17 U/L for women and AST > 20 U/L for men.
FibroScan® liver stiffness measurement ≥ 8 kPa and CAP ≥ 300 dB/m.
MRI-PDFF with ≥ 8% steatosis

Key Exclusion Criteria:
Have participated in another clinical trial within the last 6 months of Screening where the patient received active treatment for NASH/MASH.
Have participated in a clinical trial for any other indication within the last 3 months or 5 half-lives of the treatment, whichever is longer.
Are pregnant or lactating women
Have a BMI < 18 kg/m2 or > 45 kg/m2.
Have had liver transplantation or plan to have liver transplantation during the study
Design Details
Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)
Masking Description: Double Blinded
The Arms and Interventions and Outcome Measures are given in the Table 1 and 2, respectively,

RESULTS
Results: the Study is on-going and topline results will be presented when they are available.

ABSTRACT N°13 2/2

Table 1: Arms and Interventions

Participant Group/Arm	Intervention/Treatment
Experimental: Experimental Patients who meet the entry criteria for study with NA-941 will be enrolled to receive 50 mg of daily for 48 weeks.	Drug: NA-941 50 mg daily taken orally
Placebo Comparator: Placebo Patients who meet the entry criteria for study will be enrolled to receive a matching placebo twice a week for 48 weeks.	Drug: Placebo Matching placebo for oral dosing

Table 2: Outcome Measures

Primary Outcome Measures

Outcome Measure	Time Frame
Percent relative change from Baseline in liver-fat content assessed by MRI-PDFF.	Week 24

Secondary Outcome Measures

Outcome Measure	Time Frame
Change in liver stiffness and Controlled Attenuation Parameter (CAP) by FibroScan.	Week 24 and 48
Change in absolute body weight	Week 24 and 48
Change in lipids - total cholesterol, HDL, LDL, VLDL, TG, serum free fatty acids, apolipoproteins.	Week 24 and 48
Change in Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT)	Week 24 and 48
Change in ELF, Pro-C3 and other markers of liver fibrosis	Week 24 and 48
Change in HbA1c	Week 24 and 48
Change in HOMA-IR	Week 24 and 48
Change in plasma glucose	Week 24 and 48
Percent relative change from Baseline in liver-fat content by MRI-PDFF.	Week 6, Week 48
Absolute change from Baseline in liver-fat content by MRI-PDFF.	Week 6, 24, 48

ABSTRACT N°14 1/2

TITLE: CLINICAL TRIALS OF NA-931 AND NA-941 FOR THE TREATMENT OF OBESITY AND MASH

AUTHORS
Dr. Lloyd Tran, Biomed Industries, Inc
Ms. Fern Vu, Biomed Industries, Inc
Dr. Zung Tran, Biomed Industries, Inc

KEYWORDS
NA-931, NA-941, OBESITY, MASH, BIOMED

OBJECTIVES
NA-931 and NA-941 are investigational insulin-like growth factor-1 (IGF-1) analogues/metabolites that activate IGF-1, GLP-1, GIP, and glucagon receptors ("quadruple agonism"). By suppressing de novo lipogenesis and enhancing beta-oxidation, they may lower hepatic fat, promote weight loss, and improve metabolic health.

METHODS
NA-931 OBESITY TRIAL—Phase II, 13-week, randomized, double-blind, placebo-controlled, parallel-group study in adults with obesity (BMI ≥30 kg/m2) or overweight (BMI ≥27 kg/m2) plus ≥1 weight-related comorbidity (N=125). Participants received once-daily oral NA-931 (multiple dose levels including 150 mg) or placebo. ClinicalTrials.gov: NCT06564753.

Key Inclusions:
Age ≥18 years of age
Body mass index (BMI) ≥30 kg/m2 or ≥27 kg/m2, and BMI <40 kg/m2 with at least one of the following weight-related comorbidities: hypertension, dyslipidemia, or cardiovascular disease (CVD).

NA-941 MASH TRIAL—Phase II, 48-week, randomized, double-blind, placebo-controlled study in adults with biopsy-confirmed MASH and fibrosis stage 2 or 3 (N=180). Participants receive once-daily oral NA-941 (50 mg) or placebo.
Key Inclusions:
Histological diagnosis of MASH with NAS ≥ 4 and NASH-CRN fibrosis score of 2 or 3.
AST > 17 U/L for women and AST > 20 U/L for men.
FibroScan® liver stiffness measurement ≥ 8 kPa and CAP ≥ 300 dB/m.
MRI-PDFF with ≥ 8% steatosis

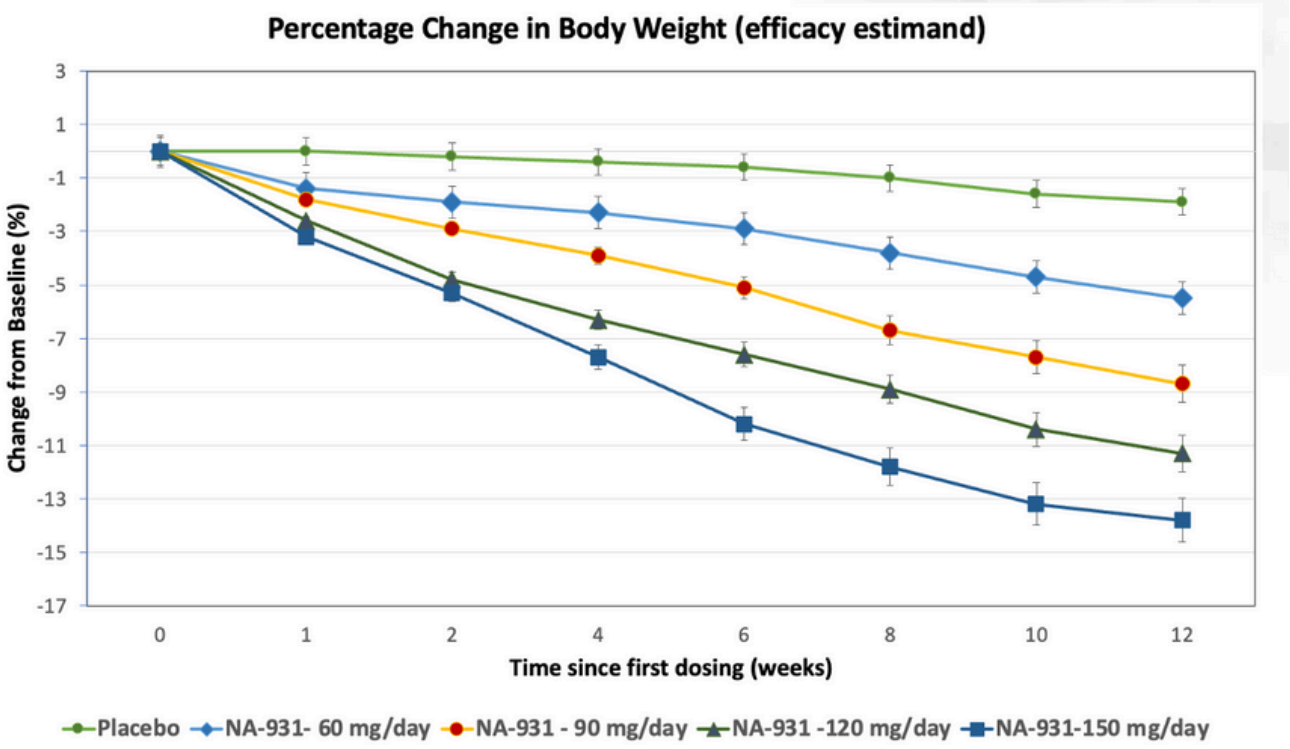
Key Exclusions:
Have participated in another clinical trial within the last 6 months
Are pregnant or lactating women
Have a BMI < 18 kg/m2 or > 45 kg/m2.

RESULTS
NA-931 produced dose-dependent mean body-weight (BW) reductions to Week 13; the 150-mg cohort achieved -13.8% BW from baseline (-12.4% vs placebo). In an exploratory responder analysis, up to 72% of NA-931–treated participants achieved ≥12% BW loss vs 2% with placebo. Treatment-emergent adverse events were mild. Gastrointestinal events were mostly insignificant or mild (83% insignificant); mild nausea/vomiting occurred in 7.3% and diarrhea in 6.3% of NA-931 recipients. No muscle loss and no clinically meaningful GI differences vs placebo were observed.

CONCLUSIONS
NA-931 yielded substantial, dose-responsive weight loss with favorable tolerability over 13 weeks. NA-941 is under evaluation for MASH with stage 2–3 fibrosis. These quadruple-pathway IGF-1 analogues represent promising therapeutic candidates for obesity and MASH.

ABSTRACT N°14 2/2

EFFICACY- Phase 2 of NA-931 in participants who are obese, with at least one weight-related co-morbid condition



EFFICACY- Phase 2 of NA-931 in participants who are obese, with at least one weight-related co-morbid condition

Multiple Ascending Dose Level	Placebo (n=29)	NA-931 60 mg (n=24)	NA-931 90mg (n=24)	NA-931 120 mg (n=24)	NA-931 150 mg (n=24)
Mean baseline body weight	96.2 kg	96.8 kg	97.9 kg	100.3 kg	99.8 kg
Mean change from baseline body weight	-1.8 kg	-5.3kg	-9.2 kg	-11.3 kg	-13.8 kg
Mean percent change from baseline	-1.9%	-5.5%	-8.7%	-11.3%	-13.8%
Placebo-adjusted mean percent change from baseline	-	-3.6%	-6.8%	-9.4%	-11.9%
p-value vs. placebo	-	-	-	0.002	0.001

ABSTRACT N°15

TITLE: UTILITY OF FIBROSCAN CAP SCORE IN MONITORING MASH: POST-HOC DATA FROM THE ENLIVEN STUDY

AUTHORS

Dr. Rohit Loomba, NAFLD Research Center, Division of Gastroenterology and Hepatology, Department of Medicine, University of California San Diego, La Jolla, CA
Dr. Philip N Newsome, Roger Williams Institute of Liver Studies, Faculty of Life Sciences and Medicine, King's College London, Foundation for Liver Research and King's College Hospital, London.
Dr. Cynthia L Hartsfield, 89bio, San Francisco, CA
Dr. Shibao Feng, 89bio, San Francisco, CA
Dr. Hank Mansbach, 89bio, San Francisco, CA
Dr. Mildred D Gottwald, 89bio, San Francisco, CA
Dr. Maya Margalit, 89bio, San Francisco, CA

KEYWORDS

CAP SCORE, MRI-PDFF, MASH, ENLIVEN

OBJECTIVES

A ≥ 30% reduction in magnetic resonance imaging-proton-density fat fraction (MRI-PDFF) has been associated with histological improvement in MASH. However, MRI-PDFF is expensive and not widely available in clinical practice. The Fibroscan controlled attenuation parameter (CAP) score is less costly to obtain, readily available at point of care, useful to support a MASLD diagnosis and is a key component of the FAST score used to assess risk of MASH. However, the utility of CAP in monitoring on-treatment changes remains unclear. The objective of this post-hoc analysis was to assess the performance of CAP score changes to predict MASH-related histological changes or ≥ 30% reduction in MRI-PDFF.

METHODS

The study included 161 patients with biopsy-confirmed MASH from the Phase 2b ENLIVEN trial with MRI-PDFF, CAP and liver biopsy at baseline and 24 weeks. The analyses were based on pooled data (all pegozafermin doses and placebo). Area under the curve (AUC) values were obtained from receiver operating characteristic (ROC) curves to assess the diagnostic performance of CAP changes to detect MASH resolution, ≥ 2pt NAS improvement and ≥30% relative reduction in MRI-PDFF. The Youden Index was used to identify optimal cutoff values.

RESULTS

The AUC of CAP absolute and percent change to predict reduction ≥30% in MRI-PDFF was 0.79 and 0.80 respectively, with optimal cut-offs of -14 dB/m for absolute change and -4.1% for percent change. CAP did not perform well in discriminating MASH resolution or a ≥2 point NAS score reduction: For MASH resolution, AUC was 0.60 (95% CI 0.48-0.73) for absolute change and 0.61 (95% CI 0.49-0.73) for percent change; for ≥2 point NAS score reduction AUC was 0.71 (95% CI 0.63-0.79) and 0.71 (95% CI 0.63-0.79) for absolute and percent change in CAP, respectively.

CONCLUSIONS

In this study, CAP score change did not correlate sufficiently with either MRI-PDFF ≥30% reduction (AUC was acceptable, but identified thresholds were within the CAP variability range and sensitivity was moderate) or histologic change in MASH. Additional studies are needed to evaluate the generalizability of these findings on the utility of CAP for disease monitoring in MASH.

ABSTRACT N°16 1/3

TITLE: PATIENT-REPORTED EXPERIENCE OF SCREENING AND EVALUATION FOR MASLD IN CHILDREN WITH OBESITY AND OVERWEIGHT

AUTHORS

Drs Anne-Sophie R. Stroes, Department of Paediatric Gastroenterology, Emma Children's Hospital, Amsterdam UMC, location University of Amsterdam, Amsterdam, The Netherlands
Dr Laura Draijer, Department of Paediatric Gastroenterology, Emma Children's Hospital, Amsterdam UMC, location University of Amsterdam, Amsterdam, The Netherlands
Dr Malika Chegary, Department of Paediatrics, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands
Dr Felix Kreier, Department of Paediatrics, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands
Drs Erim van Os, Department of Paediatrics, Rode Kruis Ziekenhuis, Beverwijk, The Netherlands
Dr Joery Goede, Department of Paediatrics, Spaarne Gasthuis, Haarlem, The Netherlands
Dr Venje Boonstra, Department of Paediatrics, BovenIJ Ziekenhuis, Amsterdam, The Netherlands
Dr Ilse Westerbeek, Department of Paediatrics, Amstelland Ziekenhuis, Amsterdam, The Netherlands
Dr Saskia Bouma, De Kinderartsenpraktijk, Amsterdam, The Netherlands
Dr Meeike Kusters, Department of Paediatrics, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands
Drs Roosje Roelants, Department of Paediatrics, Flevoziekenhuis, Almere, The Netherlands
Prof Dr Ulrich H.W. Beuers, Department of Gastroenterology and Hepatology, Amsterdam University Medical Centre, University of Amsterdam, Amsterdam, the Netherlands
Dr Adriaan G. Holleboom, Department of Vascular Medicine, Amsterdam University Medical Centre, Amsterdam, the Netherlands
Dr Marc A. Benninga, Department of Paediatric Gastroenterology, Emma Children's Hospital, Amsterdam UMC, location University of Amsterdam, Amsterdam, The Netherlands
Dr Bart G.P. Koot, Department of Paediatric Gastroenterology, Emma Children's Hospital, Amsterdam UMC, location University of Amsterdam, Amsterdam, The Netherlands

KEYWORDS

MASLD, PEDIATRIC, SCREENING, DISCOMFORT, PATIENT-EXPERIENCE

OBJECTIVES

Metabolic dysfunction-Associated Steatotic Liver Disease (MASLD) is the leading cause of chronic liver disease in children in industrialized countries, closely linked to the global rise in childhood obesity. Effective screening for this insidious disorder is crucial, yet data on the acceptability of MASLD screening in children are lacking. This study aims to evaluate self-reported discomfort in children undergoing screening and evaluation for MASLD that includes vibration-controlled transient elastography (VCTE) and shear-wave elastography (SWE).

METHODS

This cross-sectional cohort study included children (8-18 years) with overweight or obesity who were referred for MASLD evaluation following detection of elevated ALT during standard comorbidity screening. Children subsequently underwent anthropometric measurements, blood sampling, VCTE, and SWE in an outpatient hospital setting. Discomfort was assessed using the validated ‘Discomfort in Research with Children’ (DISCO-RC) questionnaire (scale 1-5) before and after the visit. Additional items assessed worry about the visit and knowledge of what to expect.

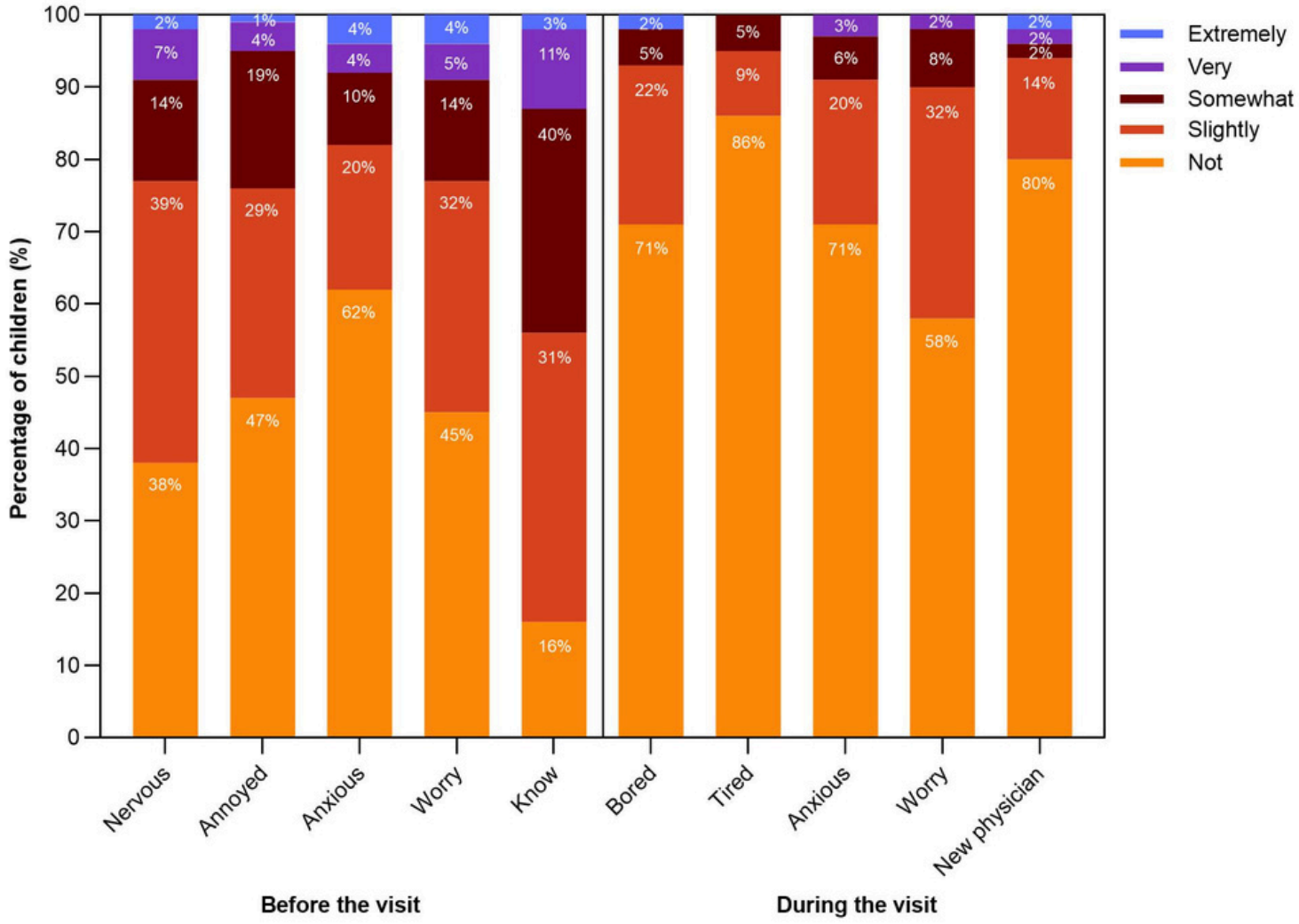
ABSTRACT N°16 2/3

RESULTS

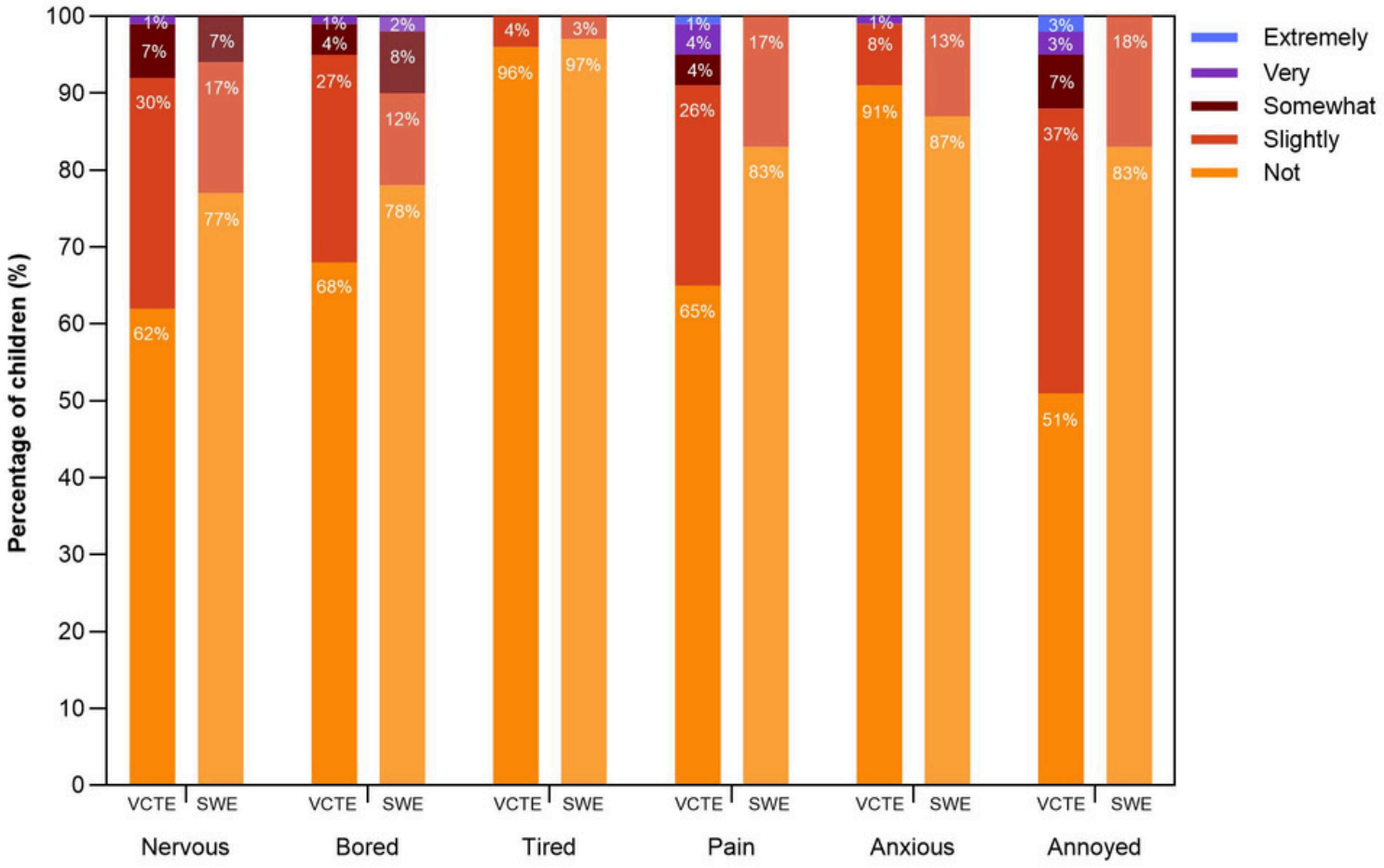
118 children (mean age 13 years) were included. Discomfort related to the MASLD screening was low, with median scores per domain 1-2 (indicating "no" to "slight" discomfort) before the MASLD evaluation visit and 1 during the visit. Before the visit, 76-82% of children reported “no” to “slight” discomfort across domains; during the visit, this was 91-95%. Over half of children (55%) had scores indicating "somewhat" to "extreme" anticipatory worry regarding what would happen during the visit, and the vast majority (87%) had scores indicating "not" or only "slightly" knowing what to expect. After the visit, the majority (90%) had scores of "not" or "slightly" worried about test results. Discomfort during VCTE and SWE procedures was also low (median score 1 per domain, indicating "no" discomfort), but total discomfort was higher for VCTE than SWE (8 [IQR 6,9] versus 7 [IQR 6,8] p<0.001, respectively).

CONCLUSIONS

Screening and subsequent evaluation for MASLD including VCTE or SWE for liver fibrosis assessment is associated with minimal discomfort and is highly acceptable to children, supporting this screening strategy in pediatric clinical practice. Our results highlight opportunities to further optimize the screening experience, most importantly through improved information delivery.



ABSTRACT N°16 3/3



ABSTRACT N°17 1/2

TITLE: LXRA INHIBITION ATTENUATES HEPATIC STEATOSIS BUT EXACERBATES INFLAMMATION: A COMPLEX THERAPEUTIC PARADIGM

AUTHORS

Dr Arnaud Dance, Medical Research Council (MRC) Metabolic Diseases Unit, Institute of Metabolic Science, University of Cambridge, Cambridge, UK.
Dr Sam Lockhart, Wellcome-Wolfson Institute of Experimental Medicine, Queen's University Belfast, Belfast
Mr Matteo Mastantuoni, Medical Research Council (MRC) Metabolic Diseases Unit, Institute of Metabolic Science, University of Cambridge, Cambridge, UK.
Dr Anthony P. Coll, Medical Research Council (MRC) Metabolic Diseases Unit, Institute of Metabolic Science, University of Cambridge, Cambridge, UK.
Sir Pr Stephen O'Rahilly, Medical Research Council (MRC) Metabolic Diseases Unit, Institute of Metabolic Science, University of Cambridge, NIHR Cambridge Biomedical Research Centre, Cambridge

KEYWORDS

FIBROSIS, LRX, CHOLESTEROL

OBJECTIVES

Our previous work showed that LXRα loss-of-function promotes liver injury and cholesterol crystal formation in the absence of lipid droplets. Since LXRα-driven de novo lipogenesis (DNL) may prevent cholesterol crystallization by enabling its esterification, targeting DNL could have dual effects, potentially beneficial for MASLD but possibly promoting progression to NASH. This project aims to assess how modulating LXRα to reduce DNL impacts hepatic cholesterol homeostasis and disease outcomes.

METHODS

Wild-type (WT) mice were treated with daily intraperitoneal injections of an LXR inverse agonist for two weeks while being fed a high-fat, high-cholesterol (HFHC) diet. Parallel groups of WT mice were fed either a low-fat, high-cholesterol (LFHC) diet or the HFHC diet alone. At the end of the dietary interventions, mice were sacrificed, and blood and liver tissues were analyzed for markers of inflammation and fibrosis.

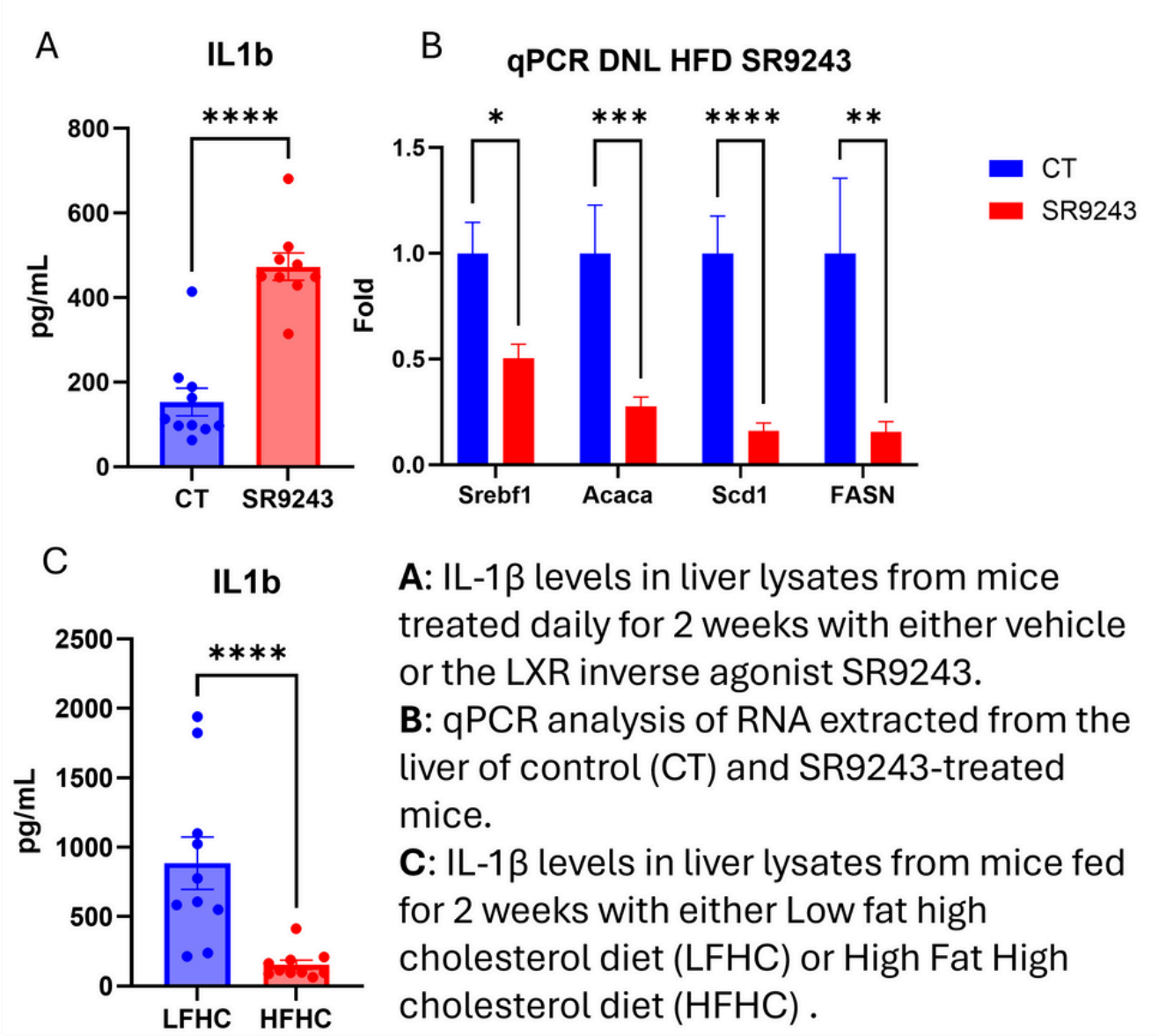
RESULTS

Treatment with the LXR inverse agonist led to a reduction in key components of the de novo lipogenesis pathway, similar to the effects observed in mice carrying a dominant-negative LXRα mutation. Additionally, the treatement induced hepatotoxicity, as evidenced by elevated circulating transaminases, increased hepatic inflammatory markers, and splenomegaly. A modest increase in fibrotic markers was also observed over the short treatment period.
Interestingly, mice fed a LFHC diet displayed increased hepatic inflammation comparable to that observed in LXR inverse agonist-treated mice.

CONCLUSIONS

Our findings demonstrate that pharmacological inhibition of LXR activity mimics key features of genetic LXRα loss-of-function, including suppression of DNL and increased susceptibility to cholesterol-induced liver injury. These results underscore the complex role of LXRα in maintaining hepatic cholesterol homeostasis, particularly under cholesterol-enriched conditions. While targeting LXR-dependent DNL may offer therapeutic potential for metabolic liver disease, our data suggest it may also carry the risk of exacerbating hepatic inflammation and early fibrogenesis in cholesterol-rich contexts.
Further studies are needed to carefully balance the therapeutic benefits of LXRα modulation against the potential risks of exacerbating liver inflammation and fibrosis in cholesterol-rich conditions, such as those seen with a Western diet.
Fibrosis, LRX, Cholesterol

ABSTRACT N°17 2/2



A: IL-1β levels in liver lysates from mice treated daily for 2 weeks with either vehicle or the LXR inverse agonist SR9243.
B: qPCR analysis of RNA extracted from the liver of control (CT) and SR9243-treated mice.
C: IL-1β levels in liver lysates from mice fed for 2 weeks with either Low fat high cholesterol diet (LFHC) or High Fat High cholesterol diet (HFHC) .

ABSTRACT N°18

TITLE: TWO-YEAR RESMETIROM THERAPY IMPROVES LIVER STIFFNESS, FIBROSIS INDICATORS, SCORES, AND REDUCES PORTAL HYPERTENSION RISK.

AUTHORS

Phil Newsome, Roger Williams Institute of Liver Studies, Faculty of Life Sciences and Medicine, King's College London, Foundationfor Liver Research and King's College Hospital, London, United Kingdom; College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom
Naim Alkhouri, Arizona Liver Health , Phoenix Arizona, United States
Rebecca Taub, Madrigal Pharmaceuticals, West Conshohocken Pennsylvania, United States
Dominic Labriola, Madrigal Pharmaceuticals, West Conshohocken Pennsylvania, United States
Xiaomin Lu, Madrigal Pharmaceuticals, West Conshohocken Pennsylvania, United States
Sam Moussa, University of Arizona for Medical Sciences, Tucson Arizona, United States
Mazen Noureddin, Houston Research Institute, Houston Texas, United States

KEYWORDS

RESMETIROM, MASH, CIRRHOSIS, FIBROSIS, BIOMARKERS

OBJECTIVES

Resmetirom, a selective thyroid hormone receptor beta agonist, is an approved therapy for metabolic dysfunction-associated steatohepatitis (MASH) with moderate to advanced liver fibrosis based on improvement in both NASH and fibrosis. MASH cirrhosis with clinically significant portal hypertension (CSPH) leads to major adverse liver outcomes. This analysis aimed to assess the effect of resmetirom over two years of treatment in 122 patients with MASH cirrhosis, with and without CSPH, as defined by Baveno VII criteria.

METHODS

A total of 122 patients with Child Pugh A MASH cirrhosis (based on MASH F4 on historic biopsy >66% or clinical diagnosis) were treated with 80 mg resmetirom for up to 2 years (MAESTRO-NAFLD-1(NCT04197479) year 1; open-label extension trial (NCT04951219) (year 2)). Patients were assessed for baseline CSPH (Baveno VII) with FibroScan vibration-controlled transient elastography (VCTE), platelet count and confirmed using magnetic resonance elastography (MRE). Non-invasive biomarkers and imaging were analysed at baseline and out to 2 years. Results are presented as mean change or % change from baseline.

RESULTS

Baseline characteristics and outcomes (changes from baseline) are listed in the Table. At baseline, 63% of patients were categorized as probable/definitive CSPH (Baveno VII), and at 1 and 2 years, respectively, 20% and 28% of CSPH positive patients no longer met criteria for CSPH. 35% of patients with confirmed F4 at baseline (liver biopsyF4 and/or platelets < 140/MRE≥5 with VCTE≥15) showed a transition from F4 to F3 at year 2 (VCTE <15 and ≥25% decrease from baseline). Discontinuation rate was 8%. Mild gastrointestinal disorders were the most common adverse events.

CONCLUSIONS

At 2 years of treatment, resmetirom demonstrated significant improvements in non- invasive biomarkers, liver stiffness on imaging and portal hypertension risk in patients with MASH cirrhosis. Resmetirom was safe and well-tolerated in this population. These findings highlight the potential of resmetirom to demonstrate clinical benefit in MAESTRO-NASH OUTCOMES, an ongoing 845 MASH cirrhosis patient clinical outcome study.

ABSTRACT N°19

TITLE: IMPACT OF RESMETIROM ON END-STAGE LIVER DISEASE IN NONCIRRHOTIC METABOLIC-ASSOCIATED STEATOHEPATITIS (MASH)

AUTHORS

Dr John O'Donnell, Madrigal Pharmaceuticals, Inc., Pennsylvania, United States.
Dr Yestle Kim, Madrigal Pharmaceuticals, Inc., Pennsylvania, United States.
Ms. Victoria Zaitceva, Optimax Access, University of Southampton Science Park, Chilworth, Hampshire, UK
Dr Mehdi Javanbakht, Optimax Access, University of Southampton Science Park, Chilworth, Hampshire, UK
Dr Amir Ansaripour, Optimax Access, Hofplein, Rotterdam, The Netherlands

KEYWORDS

MASH, NONCIRRHOTIC, DCC, HCC, RESMETIROM

OBJECTIVES

Advanced liver-related complications such as cirrhosis (F4), decompensated cirrhosis (DCC), hepatocellular carcinoma (HCC), and liver-related mortality are key drivers of morbidity and mortality in patients with MASH. This model assessed the potential impact of resmetirom compared with standard of care (SoC) on the incidence of liver-related complications in patients with MASH in the USA.

METHODS

Data from the Phase 3 MAESTRO-NASH trial informed a microsimulation model of MASH progression in patients with baseline F2 (39%) or F3 (61%) fibrosis. A cohort of 10,000 patients was simulated reflecting the baseline characteristics of the MAESTRO-NASH population. The model captured transitions between fibrosis stages (F0-F4) and between active MASH and MASH resolution, allowing for both fibrosis progression and regression over time. Also incorporated was progression to advanced liver-related complications following progression to F4. Fibrosis progression and regression probabilities in the SoC arm were based on a meta-analysis of placebo arms from prior randomized controlled trials. Relative risks reported in MAESTRO-NASH trial were used as transition probabilities for the resmetirom arm. The model estimated incidence of key outcomes: F4, DCC, HCC, liver transplantation, and liver-related mortality using Cox proportional hazards models with robust standard errors.

RESULTS

The model projected resmetirom to have reduced incidence of advanced liver-related complications compared with SoC. Lower rates of progression to F4, DCC, HCC, and liver-related mortality in the resmetirom arm were observed. These benefits were supported by hazard ratios derived from simulated population: F4 [HR=0.484; 95% confidence interval (CI): 0.45–0.52; p<0.01], DCC [HR=0.540; 95%CI: 0.47-0.63; p<0.01], HCC [HR=0.464; 95%CI: 0.39–0.55; p<0.01], candidate for liver transplantation [HR=0.519; 95%CI: 0.44–0.61; p<0.01], and liver-related mortality [HR=0.51; 95%CI: 0.46–0.56; p<0.01]. These findings reflect consistent and statistically significant reductions in major clinical risks with resmetirom.

CONCLUSION

In lieu of a completed confirmatory trial, the model projected resmetirom to potentially reduce the risk of advanced liver-related complications in MASH patients with moderate to advanced fibrosis. These reductions may lead to improvements in healthcare resource utilization, costs, life expectancy, and quality of life. Further research and confirmatory trials are warranted to confirm resmetirom effectiveness in reducing incidence of clinical events.

ABSTRACT N°20

TITLE: NATURAL HISTORY AND PROGRESSION OF MASH: A U.S. CLAIMS-BASED ANALYSIS USING OPTUM MARKET CLARITY DATA

AUTHORS

DR. YESTLE KIM, Madrigal Pharmaceuticals, Inc., West Conshohocken, PA, USA
DR. ROMINA FAKHRAEI, Broadstreet HEOR, Vancouver, BC, Canada
DR. JOHN O'DONNELL, Madrigal Pharmaceuticals, Inc., West Conshohocken, PA, USA
DR. KARISSA JOHNSTON, Broadstreet HEOR, Vancouver, BC, Canada
ROSIE SUN, Broadstreet HEOR, Vancouver, BC, Canada
MELISSA BATHER, Broadstreet HEOR, Vancouver, BC, Canada
REEM MUSTAFA, Broadstreet HEOR, Vancouver, BC, Canada
ANDREW KENNEDY, Broadstreet HEOR, Vancouver, BC, Canada
DR. AMREEN DINANI, Duke University Health System, NC, USA

KEYWORDS

MASH; REAL-WORLD; DISEASE PROGRESSION; ESLD

OBJECTIVES

Metabolic dysfunction-associated steatohepatitis (MASH) is a progressive liver disease characterized by hepatic steatosis, inflammation, and varying degrees of fibrosis.1 This study aimed to (1) characterize patients diagnosed with MASH, and (2) evaluate their progression to end stage liver disease (ESLD).

METHODS

This retrospective cohort study was conducted using Optum's® de-identified Market Clarity Data in the United States (January 1, 2019, to December 31, 2024). Adult patients were included if they had ≥1 inpatient or ≥2 outpatient diagnoses of MASH on separate dates. A 2-year lookback period was used to assess baseline ESLD, identified using diagnostic and procedural codes for compensated cirrhosis (CC), decompensated cirrhosis (DC), hepatocellular carcinoma (HCC), or liver transplant (LT). Patients without ESLD at baseline were followed to evaluate progression to any ESLD outcome during the follow-up period.

RESULTS

A total of 21,894 patients with MASH were included. Of these, 14,612 (66.7%) had no evidence of ESLD at baseline (mean age: 56.4 years) and were followed for median of 2.34 years (IQR: 1.67–3.13) to assess progression. Non-invasive testing (NIT) was the most common method for fibrosis staging at diagnosis (18.2%), most frequently; abdominal ultrasound (9.0%), FibroScan (5.7%) and CT scan (4.1%); while 3.7% underwent liver biopsy. Cardiometabolic conditions were highly prevalent, including obesity (69.3%), dyslipidemia (77.8%), hypertension (58.1%), type 2 diabetes (39.3%), and metabolic syndrome (38.2%), with 81.8% of patients having >2 risk factors. Among patients without baseline ESLD, 2,431 (16.6%) progressed during follow-up: 467 (3.2%) to CC, 1,902 (13.0%) to DC, 48 (0.3%) to HCC, and 14 (0.1%) to LT. The average time to the first progression event was 13.1 months. Patients who progressed to ESLD had higher inpatient utilization—18.1% had at least one admission compared to 5.0% of non-progressors—and incurred greater healthcare costs, with median annual costs of $90,253 USD versus $48,808 USD.

CONCLUSIONS

In this large real-world cohort of patients with MASH, a notable proportion progressed to advanced liver outcomes over a relatively short follow-up period. These findings underscore the importance of early identification and targeted management strategies to prevent ESLD progression, which may help reduce inpatient utilization and associated healthcare costs.

ABSTRACT N°21

TITLE: PREVALENCE AND PREDICTORS OF HEPATIC STEATOSIS IN PATIENTS UNDERGOING SLEEVE GASTRECTOMY : A BIOPSY-PROVEN STUDY

AUTHORS

Dr Riham Soliman, Tropical Medicine Department, Faculty of Medicine, Port Said University, Port Said, Egypt. 2 Egyptian Liver Research Institute and Hospital (ELRIAH), Mansoura, Egypt.
Dr Ahmed Helmy, Tropical Medicine and Gastroeneterology Department, Faculty of Medicine, Assiut University, Assiut, Egypt.
Dr Nabiel Mikhail, Biostatistics and Cancer Epidemiology Department, South Egypt Cancer Institute, Assiut University, Assiut, Egypt.
Dr Helmy Ezzat, Gastrointestinal Surgery Center, Faculty of Medicine, Mansoura University, Egypt.
Dr Ahmed Mehrez, General Surgery Department, Faculty of Medicine, Delta University for Science and Technology, Egypt.
Dr Ebrahim Abdel Halim, Surgery Department, Faculty of Medicine - Horus University, Egypt.
Prof Khaled Zalata, Pathology Department, Faculty of Medicine, Mansoura University, Mansoura, Egypt.
Prof Rokia Masoud, General Surgery Department, Faculty of Medicine, Delta University for Science and Technology, Egypt.
Dr Ayman Hassan, Higher Institute of Applied Medical Science, Sherbin, Mansoura, Egypt.
Dr Ahmed Farahat, Egyptian Liver Research Institute and Hospital (ELRIAH), Mansoura, Egypt.
Dr Mohamed El Emam, Egyptian Liver Research Institute and Hospital (ELRIAH), Mansoura, Egypt.
Prof Mohamed Elbasiony, Gastroenterology and Hepatology Unit, Internal Medicine Department, Faculty of Medicine, Mansoura University, Mansoura, Egypt.
Prof Gamal Shiha, Egyptian Liver Research Institute and Hospital (ELRIAH), Mansoura, Egypt. Gastroenterology and Hepatology Unit, Internal Medicine Department, Faculty of Medicine, Mansoura University, Mansoura, Egypt.

KEYWORDS

STEATOHEPATITIS, BIOPSY, CAP, BARIATRIC SURGERY.

OBJECTIVES

To date, there is a lack of population-based studies assessing the prevalence and severity of steatosis and metabolic-associated steatohepatitis (MASH) in Egypt. CAP is widely used as a non-invasive tool for hepatic steatosis assessment, yet its reliability in obese populations remains unclear. We aimed to examine the prevalence and risk factors for steatosis and steatohepatitis in Egyptian patients undergoing laparoscopic sleeve gastrectomy and evaluate CAP’s diagnostic accuracy against liver biopsy in detecting hepatic steatosis.

METHODS

In this prospective cross-sectional study (2019–2023), 162 obese adults undergoing barianevertric surgery were enrolled. CAP was performed prior to intraoperative wedge liver biopsy. Histological grading of steatosis and NAS scoring were conducted by blinded pathologists. Diagnostic accuracy of CAP was evaluated using AUROC, sensitivity, specificity, PPV, and NPV.

RESULTS

Hepatic steatosis was present in 63.6% of patients by liver biopsy. CAP overestimated steatosis in 40% of biopsy-confirmed S0 cases, misclassifying them as S3. CAP cutoff of 286 dB/m for ≥S1, sensitivity, specificity, PPV, and NPV were 57.7%, 65.0%, 76.3%, and 44.1%, respectively (AUROC = 0.577). Only 14.2% had steatohepatitis. Multivariate analysis identified albumin (p=0.040) and hemoglobin (p=0.018) as independent protective factors.

CONCLUSIONS

CAP significantly overestimated steatosis severity highlighting its limited reliability in obese populations.

ABSTRACT N°22 1/2

TITLE: KEY DETERMINANTS OF RESMETIROM ELIGIBILITY IN HIV-POSITIVE INDIVIDUALS WITH MASLD

AUTHORS

Dr. Ahmed Kamel, Clinical Pharmacy Department, Faculty of Pharmacy, Cairo University
Dr. Amani M. Ali, Clinical Pharmacy Department, Faculty of Pharmacy, Cairo University
Dr. Rahma Mohammed, Cairo University, Cairo, Egypt, Cairo University Hospitals HIV Clinic, Endemic Medicine Department, Cairo, Egypt,
Dr. Ahmed Cordie, Cairo University, Cairo University Hospitals HIV Clinic, Endemic Medicine Department,, Cairo, Egypt,

KEYWORDS

MASLD, RESMETIROM, HCV, HIV, FIBROSCAN

OBJECTIVES

Resmetirom is currently the only approved therapy to reverse histological abnormalities commonly associated with metabolic dysfunction-associated steatotic liver disease (MASLD). We aimed to assess the number of potentially eligible patients within a cohort of MASLD PLWH receiving care at a human immunodeficiency virus (HIV) clinic in Cairo, Egypt.

METHODS

This was a retrospective cohort study the consecutively enrolled PLWH between January 2022 and December 2024. MASLD was diagnosed as per the European association for the study of the liver (EASL) guidelines. Liver stiffness measurement (LSM) and controlled attenuation parameter (CAP) were obtained via FibroScan® and categorized according to established thresholds. Resmetirom eligibility was assessed based on current treatment guidance, incorporating LSM and platelet count criteria. Univariate logistic regression was used to assess factors associated with eligibility and generalized linear mixed modelling was used to assess the change in eligibility across time.

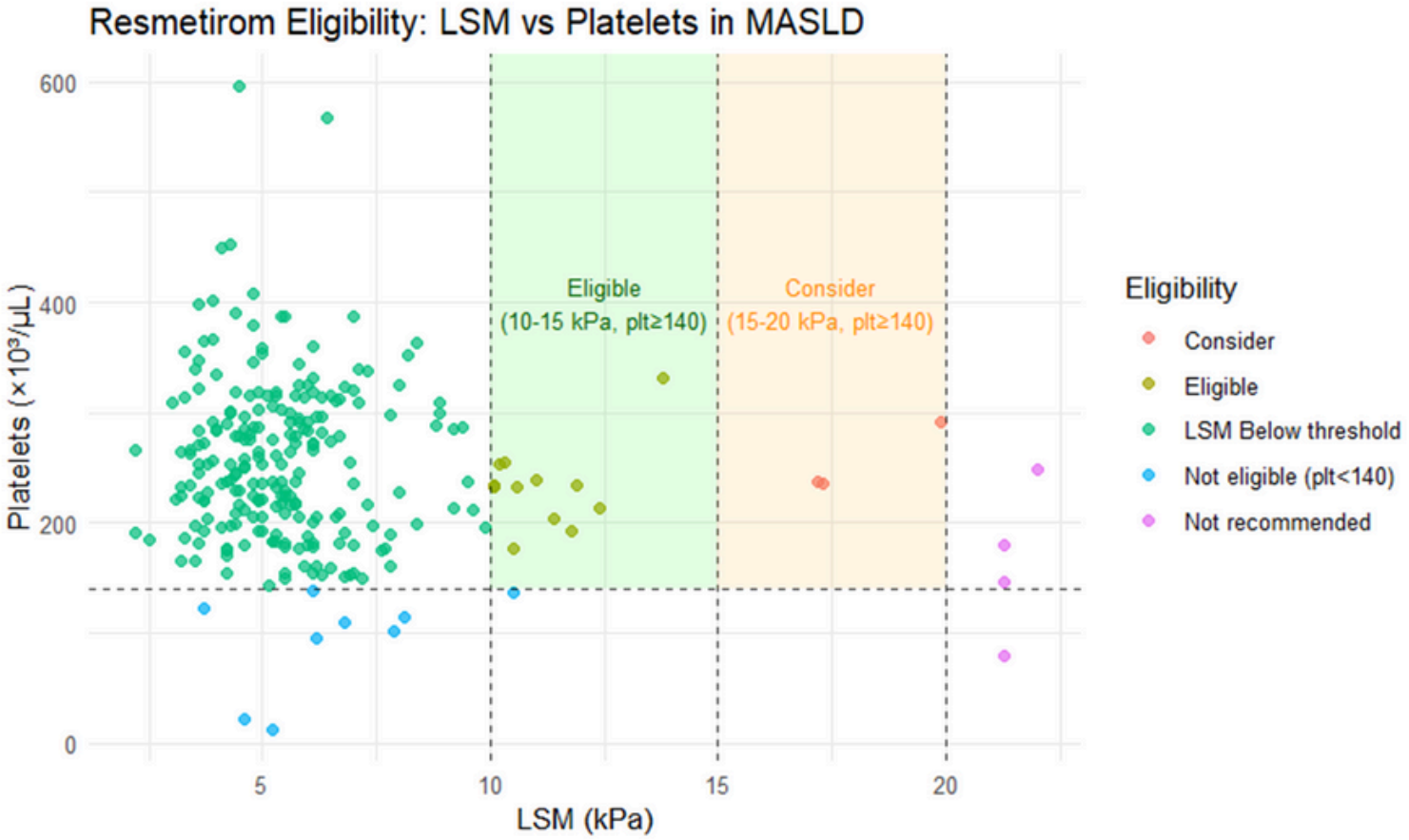
RESULTS

Among 253 PLWH with MASLD (72.7% males and mean age 39.9 ± 10.1 years), the majority (n = 219, 86.6%) had LSM below the required treatment threshold, indicating low fibrosis risk. In total, 15 patients (5.9%) were classified as eligible or treatment candidates, while 9 patients (3.6%) were not eligible due to thrombocytopenia (platelets <140×10³/μL). Compared to non-eligible individuals, eligible patients had significantly higher rates of obesity (93.3% vs 42.4%, p = 0.041), diabetes (21.7% vs 4.3%, p = 0.006), high cardiometabolic risk (≥3 factors: 66.7% vs 23.9%, p = 0.015), and COVID-19 vaccination (86.7% vs 43.8%, p = 0.029). No significant differences were found in CD4 count, viral suppression, treatment status, or HCV exposure status. Over a median follow-up of 11.6 [6.94;15.3] months, the odds of eligibility decreased by 32% per month (OR = 0.68, 95% CI: 0.47–0.98, p = 0.036).

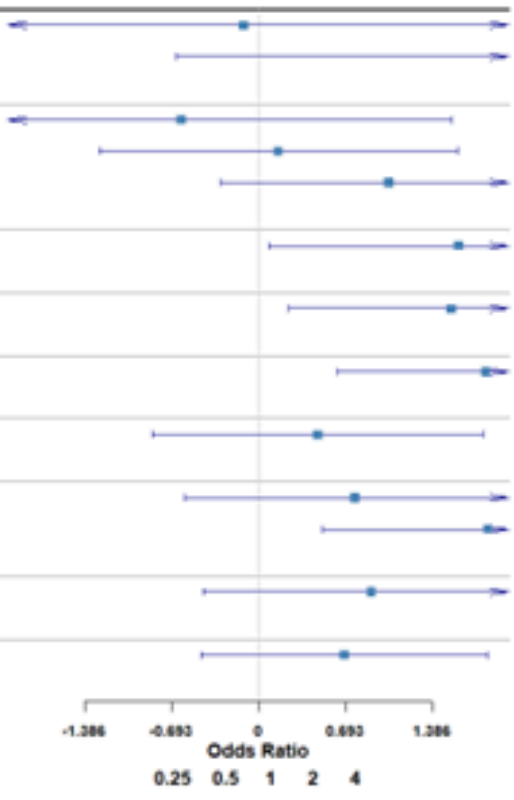
CONCLUSION

Eligibility for resmetirom was low in PLWH with MASLD and was primarily driven by severity of MASLD, and the number of cardiometabolic risk factors including obesity, and diabetes, rather than HIV-specific variables such as CD4 count, viral suppression, or HCV status. These findings emphasize that metabolic comorbidities, not HIV disease markers, determine resmetirom candidacy in this population and should guide clinical screening strategies

ABSTRACT N°22 2/2



Variable	Category	n/N (%)	OR (95% CI)	P-value
BMI Category	Overweight (25-29.9)	1/107 (0.9%)	0.89 (0.04-22.33)	1.000
	Obese (≥30)	14/115 (12.2%)	9.00 (0.52-155.19)	0.041
	Normal (<25) (Reference)	0/31 (0.0%)	1.00 (Reference)	—
CD4 Count	<200 cells/μL	1/35 (2.9%)	0.54 (0.06-4.64)	1.000
	200-349 cells/μL	3/50 (6.0%)	1.17 (0.28-4.88)	1.000
	350-499 cells/μL	4/30 (13.3%)	2.82 (0.74-10.72)	0.123
	≥500 cells/μL (Reference)	6/116 (5.2%)	1.00 (Reference)	—
COVID-19 Vaccination	Vaccinated	13/146 (8.9%)	4.94 (1.09-22.37)	0.029
	Not vaccinated (Reference)	2/103 (1.9%)	1.00 (Reference)	—
Cardiometabolic Risk	High risk (≥3 factors)	12/122 (9.8%)	4.65 (1.28-16.92)	0.015
	Low risk (<3 factors) (Reference)	3/131 (2.3%)	1.00 (Reference)	—
Diabetes Status	Yes	5/23 (21.7%)	6.11 (1.89-19.81)	0.006
	No (Reference)	10/230 (4.3%)	1.00 (Reference)	—
HCV Status	HCV exposure	3/35 (8.6%)	1.60 (0.43-5.99)	0.446
	No HCV exposure (Reference)	12/217 (5.5%)	1.00 (Reference)	—
HbA1c Category	Prediabetes (5.7-6.4%)	4/57 (7.0%)	2.16 (0.56-8.34)	0.267
	Diabetes (≥6.5%)	5/28 (17.9%)	6.22 (1.67-23.17)	0.010
	Normal (<5.7%) (Reference)	5/148 (3.4%)	1.00 (Reference)	—
Treatment Status	Treatment Naïve	3/25 (12.0%)	2.45 (0.64-9.37)	0.175
	On treatment (Reference)	12/228 (5.3%)	1.00 (Reference)	—
Viral Suppression	Detectable	6/58 (10.3%)	1.98 (0.63-6.17)	0.233
	Suppressed (Reference)	7/127 (5.5%)	1.00 (Reference)	—



ABSTRACT N°23

TITLE: REAL WORLD SEMAGLUTIDE DOSE-ESCALATION AND PERSISTENCE AMONG PATIENTS WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE [MASLD]

AUTHORS

Arushi Chadha, Medicus Economics, LLC
Avery Mohan, Medicus Economics, LLC
Dominic Nunag, Medicus Economics, LLC
Samantha Clark, Medicus Economics, LLC
Matthew Davis, Medicus Economics, LLC
Nipun Atreja, Madrigal Pharmaceuticals, Inc.
Blake Thomas, Madrigal Pharmaceuticals, Inc.
Francis Lobo, Madrigal Pharmaceuticals, Inc.

KEYWORDS

GLP-1, MASH, MASLD, DOSE-ESCALATION, PERSISTENCE

OBJECTIVES

Semaglutide 2.4 mg is being studied for MASH, a progressive MASLD subtype, in the ongoing ESSENCE trial. Interim results show 88% of participants followed the 16-week dose-escalation schedule and maintained a 2.4 mg dose at 72 weeks. This analysis evaluates real-world compliance with the ESSENCE trial protocol among MASLD patients starting semaglutide 2.4 mg for an approved indication.

METHODS

A retrospective cohort study including patients with MASLD initiating semaglutide 2.4 mg (earliest prescription defined as the index date) between 2021-2024 was conducted in Optum Market Clarity data. Patients were required to have 72 weeks of continuous enrollment. Those with evidence of other liver diseases, severe MASLD-related complications, or prior GLP-1 use during the 12-month baseline period were excluded. Eligible patients were classified into three groups based on compliance with the ESSENCE trial protocol during the 72-week follow-up: (1) Non-adherence to the dose escalation schedule (reaching 2.4 mg at 16 weeks), (2) Dose escalation followed by discontinuation (≥45-day gap in medication coverage), and (3) Dose escalation with persistence (no discontinuation). Proportion of days covered (PDC), defined as the percentage of days covered by a semaglutide 2.4 mg fill over the 72-week follow-up period, was calculated.

RESULTS

Of the 1,550 adults included in the final sample, 91.2% (n=1,413) and 11.9% (n=184) presented with obesity and type 2 diabetes, respectively. Mean (standard deviation) age was 47.3 (10.7) years and 68.1% (n=1,056) were female. Group 1 comprised 85.7% (n=1328) of patients, 62.2% (n=826) of whom discontinued prior to the end of the 16-week dose-escalation schedule. Groups 2 and 3 accounted for 6.9% (n=107) and 7.4% (n=115) of patients, respectively. Overall PDC for the 72-week follow-up period was 42.2% (32.5), with PDC in Groups 1, 2, and 3, of 36.7% (30.4), 54.3% (18.3), and 94.7% (6.2), respectively.

CONCLUSION

Less than 8% of patients with MASLD followed the ESSENCE trial dose-escalation schedule and remained persistent throughout the 72-week follow-up period. Findings suggest a lack of alignment between GLP-1 use in the ESSENCE trial and that observed for currently approved indications in the real world, with further research needed to identify the impact of suboptimal GLP-1 use on liver-related outcomes.

ABSTRACT N°24 1/2

TITLE: THE QUANTITATIVE HEPQUANT DUO TEST UNCOVERS THE FUNCTIONAL HETEROGENEITY OF ADVANCED CHRONIC LIVER DISEASE

AUTHORS

Dr. Joanne Imperial, HepQuant, LLC, Denver, CO, USA
Dr. Michael McRae, Custom DX Solutions LLC, Houston, TX, USA
Dr. Gregory Everson, HepQuant, LLC, Denver, CO, USA

KEYWORDS

MASH; MET-ALD; LIVER FUNCTION TEST

OBJECTIVES

The oral cholate challenge test (HepQuant DuO) of liver function and physiology was launched as a commercial laboratory developed test through a formal Early Access Program (EAP) in 2023–2024. We used the test to characterize the functional and physiologic heterogeneity in compensated advanced chronic liver disease (cACLD).

METHODS

The Test involved oral administration of [2,2,4,4-2H] cholic acid and blood sampling at 20 and 60 min. Serum was analyzed for cholate concentrations by LC-MS/MS. The disease severity index (DSI), a measure of liver function, and SHUNT%, a measure of portal systemic shunting, were calculated. Subjects with ALD and BMI >30 kg/m2 were defined as MetALD.

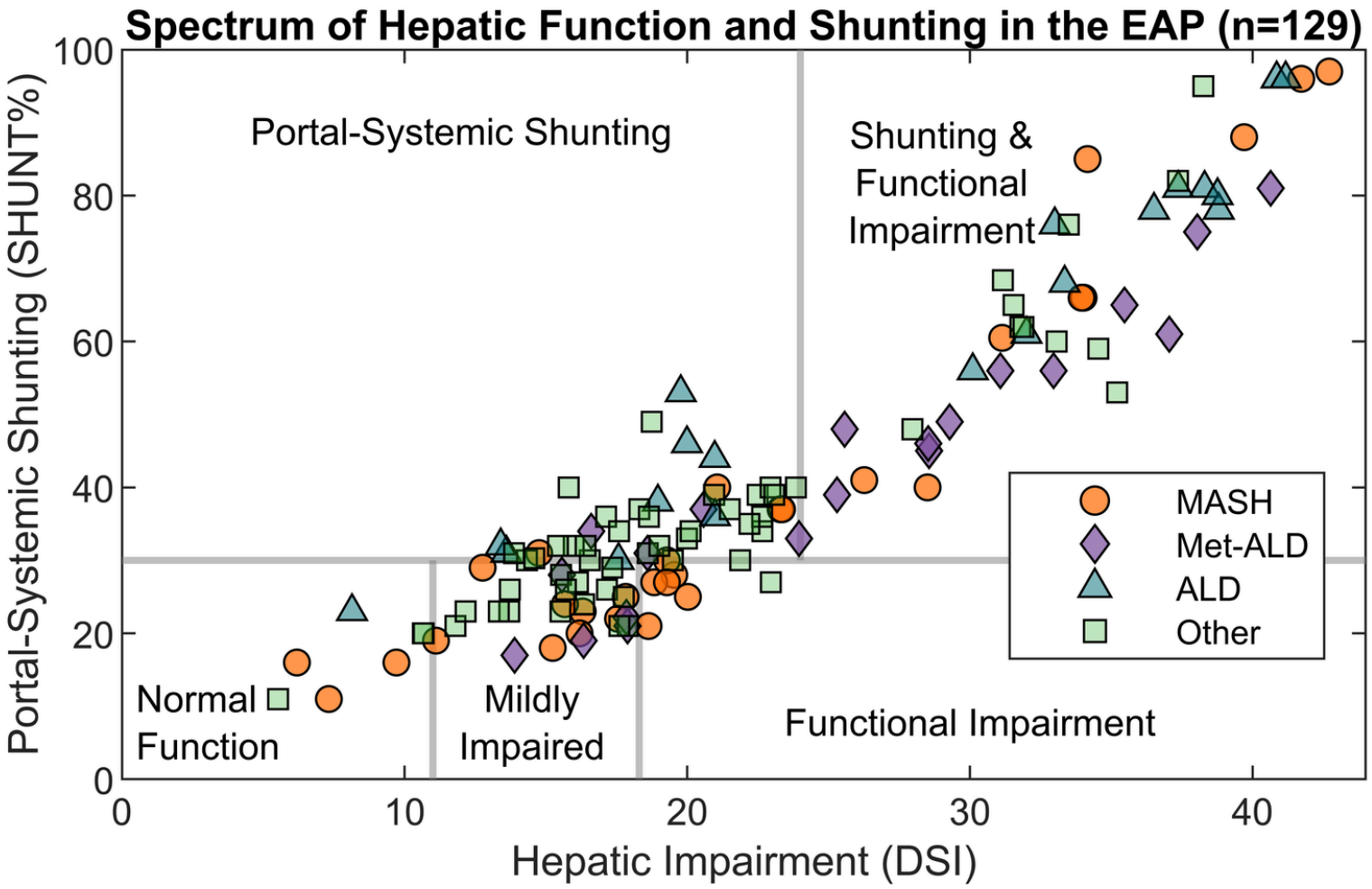
RESULTS

In the EAP, Tests were ordered for 129 patients representing a range of etiologies, including 23% MASLD/MASH, 16% alcohol-associated liver disease (ALD), and 16% MetALD, and 45% other. Patients were on average 59 ± 13 years of age, 50% female, 76% overweight or obese (BMI >25 kg/m2), and 46% obese (BMI >30 kg/m2). A wide range of functional impairment and shunting was observed. Mean (± SD) values for DSI were 21.9 ± 9.9 for MASLD/MASH, 25.7 ± 8.4 for MetALD, 27.7 ± 10.6 for ALD, and 20.8 ± 8.0 for all other etiologies. For reference, DSI was 8.4 ± 3.2 in lean controls and 12.1 ± 2.5 in overweight controls (McRae 2025). Patients were stratified by DSI (function) and SHUNT% (shunting) (Figure 1): 7 (5%) with normal function, 39 (30%) with only portal-systemic shunting, 31 (24%) with mild functional impairment, 9 (7%) with significant functional impairment, and 43 (33%) with significant functional impairment and shunting. Using the RISK ACE model (Kittelson 2025), the individual estimated 1-year risk for clinical outcome ranged from 0.3% (DSI 5.5) to 90.5% (DSI 45.4).

CONCLUSION

The Test uncovered significant heterogeneity in functional and physiologic impairment in the EAP experience. Quantitative functional assessment may be useful to assess clinical risk to inform decisions regarding the use of endoscopy to screen for varices, defining the intensity of clinical follow-up, and establish a baseline for monitoring treatment effects.

ABSTRACT N°24 2/2



ABSTRACT N°25

TITLE: A NOVEL 8-GENE SIGNATURE FOR HEPATOCYTE BALLOONING REVEALS SPP1-MEDIATED PRO-FIBROTIC CROSSTALK IN MASH

AUTHORS

Mr. DEBOPRIYO GANGULY, BRIC-NIBMG
Ms. BANDANA MONDAL, BRIC-NIBMG
Mr. AYAN MANDAL, BRIC-NIBMG
Dr. TRINATH GHOSH, BRIC-NIBMG
Ms. MONALISHA DEO, BRIC-NIBMG
Ms. MISBAH AHMED, BRIC-NIBMG
Dr. ANKITA CHATTERJEE, JCMLRIA
Dr. PRIYADARSHI BASU, BRIC-NIBMG

KEYWORDS

MASH, HEPATOCYTE-BALLOONING, SPP1, TRANSCRIPTOMICS, CELLULAR-CROSSTALK

OBJECTIVES

Hepatocyte ballooning (HB) is a key driver of fibrosis in metabolic dysfunction-associated steatohepatitis (MASH), but its diagnosis is challenging and its molecular drivers are obscure. Our objectives were twofold: 1) to identify and validate a robust, non-invasive transcriptomic signature for HB, and 2) to elucidate the underlying cellular crosstalk mechanisms that link HB to MASH progression and fibrogenesis.

METHODS

We analyzed liver transcriptomic data from 38 MASLD patients using Weighted Gene Co-expression Network Analysis (WGCNA) and machine learning (LASSO/ridge regression) to develop a predictive signature for HB. The signature was validated in an independent public cohort (GSE89632). Mechanistic insights were derived from single-nucleus RNA-sequencing (snRNA-seq) and CellChat analysis of an ALIOS diet-induced NASH mouse model (GSE189600), with key findings confirmed in vitro.

RESULTS

We identified a novel 8-gene signature that predicted HB with outstanding accuracy (AUC=0.986), significantly outperforming standard liver enzymes. This was validated in an independent cohort (AUC=0.89). In the NASH mouse model, snRNA-seq revealed the emergence of specific pro-inflammatory macrophage (Mac2) and activated stellate cell (Stellate2) populations alongside hepatocytes with a high ballooning signature score (BSSH). Pseudotime analysis positioned BSSH hepatocytes at a terminal stress trajectory. Critically, CellChat analysis uncovered a pro-fibrotic communication network orchestrated by Mac2-derived SPP1, which signals to both stressed BSSH hepatocytes and fibrogenic Stellate2 cells, driving a pathological feedback loop.

CONCLUSIONS

Our study provides a highly accurate 8-gene signature as a potent non-invasive diagnostic tool for hepatocyte ballooning in MASH. Furthermore, we identify macrophage-derived SPP1 as the central mediator of a pro-fibrotic cellular crosstalk network, revealing a novel and highly specific therapeutic target to disrupt MASH progression.

ABSTRACT N°26 1/2

TITLE: SUBGROUPING AND MONITORING FIBROSIS DYNAMICS IN MASH F3 USING AI-BASED SEPTA ANALYSIS AND DIGITAL PATHOLOGY

AUTHORS
Nikolai Naoumov, University College London, Division of Medicine, London, United Kingdom
Elaine Chng, HistoIndex Pte Ltd, Singapore
Yayun Ren, HistoIndex Pte Ltd, Singapore
Dominique Brees, Novartis Pharma AG, Basel, Switzerland
Chandra Saravanan, Novartis Institute of Biomedical Research, Cambridge, MA, United States
Dean Tai, HistoIndex Pte Ltd, Singapore
David Kleiner, National Cancer Institute, Bethesda, MD, United States
Arun Sanyal, Stravitz-Sanyal Institute of Liver Disease and Metabolic Health, Virginia Commonwealth University School of Medicine, Richmond, United States

KEYWORDS
MASH, SEPTA, DIGITAL PATHOLOGY, SHG/TPEF

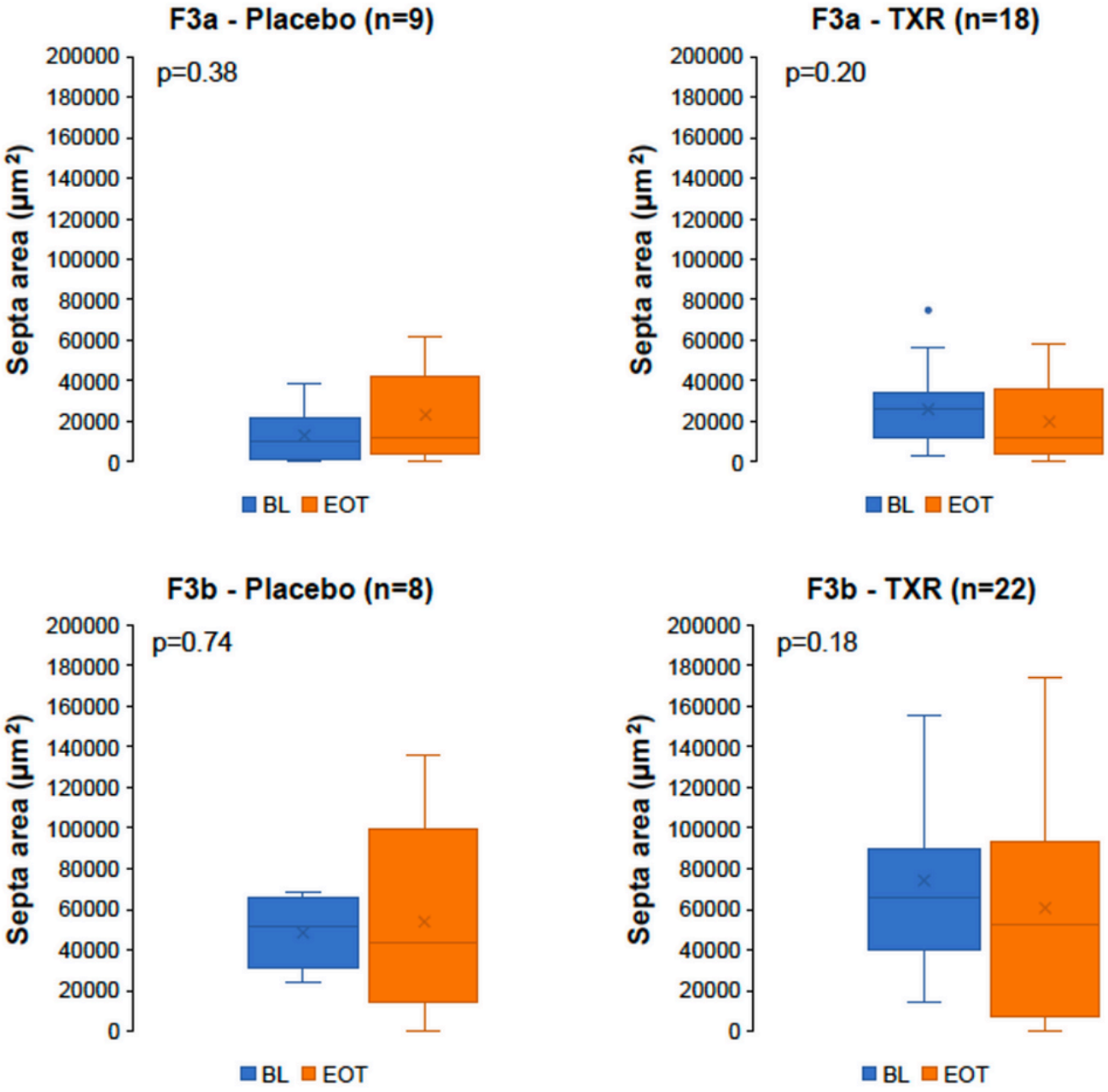
OBJECTIVES
Metabolic Dysfunction-Associated Steatohepatitis (MASH) with bridging fibrosis (stage F3) is a clinically significant but heterogeneous population, with potential for both fibrosis regression or progression. Second harmonic generation/two-photon excitation fluorescence (SHG/TPEF) microscopy combined with artificial intelligence (AI) enables sensitive and objective fibrosis quantification. This study aimed to identify subgroups within the MASH F3 population based on quantitative septa features.

METHODS
Paired liver biopsies from 57 FLIGHT-FXR trial patients (NCT02855164), all with bridging fibrosis, were analysed: placebo (PLB, n=17) and tropifexor (TXR, n=40). Unstained slides were imaged using SHG/TPEF, with 12 septa parameters quantified at baseline (BL) and end of treatment (EOT). Septum width was measured on 93 randomly selected septa to define “thick” (mean 167 µm) vs. “thin” (mean 41 µm), with a cutoff of 88.5 µm (Youden’s index). The ratio of thick septa area to total septa area per biopsy was used to define two F3 subgroups: predominantly thin septa (F3a; mean ratio 13%, range 0–48%) and predominantly thick septa (F3b; mean ratio 71%, range 51–97%).

RESULTS
At BL, 27 patients were classified as F3a (PLB, n=9; TXR, n=18) and 30 as F3b (PLB, n=8; TXR, n=22). Septa area was 3-fold larger in F3b (21,820 ± 3383 µm²) vs. F3a (6752 ± 7219 µm²; $p < 0.001$). Septa area also showed baseline imbalance between PLB and TXR arms ($p = 0.027$). Despite unchanged ordinal fibrosis stage, transitions between F3a and F3b from BL to EOT were observed in 5/11 PLB and 10/28 TXR cases. While PLB-treated patients showed no consistent septa changes, the TXR-treated F3b subgroup showed a notable, though not statistically significant, reduction in septa area. (Figure)

CONCLUSIONS
SHG/TPEF microscopy with AI provides quantitative insights into fibrosis architecture in MASH F3 patients, capturing dynamic changes undetectable by conventional histology. This digital pathology approach allows objective F3 sub-staging, which may enhance patient stratification, endpoint sensitivity, and treatment-response evaluation in clinical trials.

ABSTRACT N°26 2/2



Median septa area (lower quartile, upper quartile), µm²

		BL	EOT	p-value (BL to EOT)
F3a	Placebo	10524.4 (1329.4, 22015.5)	11474.6 (4123.7, 42553.8)	0.38
	Tropifexor	26046.6 (12326.3, 34220.4)	11977.5 (3619.2, 36068.4)	0.20
F3b	Placebo	51999.7 (30762.6, 65272.9)	43822.3 (13633.6, 99577.3)	0.74
	Tropifexor	66243.9 (39611.6, 90085.4)	52330.7 (6867.6, 93468.4)	0.18

ABSTRACT N°27 1/2

TITLE: REAL-WORLD CLINICAL CHARACTERISTICS AND TREATMENT PATTERNS OF PATIENTS WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOHEPATITIS IN GERMANY.

AUTHORS

Dr Yestle Kim, Madrigal Pharmaceuticals, West Conshohocken, PA, USA- Presenter
Dr Melinda J Daumont, Madrigal Pharmaceuticals, West Conshohocken, PA, USA
Mr Michele Intorcia, Madrigal Pharmaceuticals, West Conshohocken, PA, USA
Mrs Hayley Wallinger, Adelphi Real World, Bollington, UK
Miss Kathryn Tebbs, Adelphi Real World, Bollington, UK
Miss Rebecca Storm, Adelphi Real World, Bollington, UK
Miss Lena Amari, Adelphi Real World, Bollington, UK
Miss Emily Quiñones, Adelphi Real World, Bollington, UK

KEYWORDS

MASH, MASLD, FIBROSIS, HCRU, GERMANY

OBJECTIVES

To understand the disease journey of patients with metabolic dysfunction-associated steatohepatitis (MASH) in Germany, and to assess the need for novel treatments to prevent disease progression.

METHODS

Data were drawn from the Adelphi Real World MASH Disease Specific Programme™, a cross-sectional survey of physicians and their patients with MASH in Germany from January–May 2024. Physicians provided patient demographics and clinical characteristics. Patients were grouped by physician-stated fibrosis severity at data collection (F0–F1, F2–F3 and F4) and were compared using Spearman's Rho and Kruskal-Wallis.

RESULTS

Overall, 65 physicians provided data for 587 patients with MASH. For F0–F1 (n=344), F2–F3 (n=236), and F4 (n=7) patients, mean (± standard deviation) age was 54.7±10.2, 55.8±10.2 and 61.7±7.4 years, 40.7%, 36.4%, 28.6% were female , and body mass index was 32.1±4.0kg/m2, 32.3±4.1kg/m2 and 29.2±5.5kg/m2, respectively. As fibrosis severity increased patients had more tests to aid diagnosis (r=0.13, p<0.01), especially imaging scans (r=0.18, p<0.001), and more symptoms at diagnosis (r=0.18, p<0.001) and at data collection (r=0.22, p<0.001). Overall, the most common symptoms at diagnosis were fatigue (32.5% of F0–F1, 46.5% F2-F3 and 85.7% F4), sleep disturbance (19.1%, 25.4%, 28.6%) and general weakness (16.6%, 23.3%, 57.1%). These were most common at data collection also: fatigue (39.0% of F0–F1, 55.4% F2–F3, 85.7% F4); sleep disturbance (24.1%, 33.1%, 28.6%); and general weakness (20.2%, 33.9%, 71.4%). To assess MASH, F0–F1, F2–F3 and F4 patients had a mean of 2.7±2.6, 2.9±3.3, 1.3±0.6 liver composite tests, 2.2±1.2, 2.5±1.6, 4.1±3.4 imaging scans (r=0.10, p<0.05) and 3.0±1.8, 3.5±2.3, 5.5±3.8 blood tests (r=0.10, p<0.05) in the two years prior to survey. Increased fibrosis severity was associated with higher Charlson Comorbidity Index (r=0.95), cardiovascular risk (r=0.28), hepatocellular carcinoma risk (r=0.37), more treatments prescribed for MASH-associated comorbidities (r=0.20) and history of major adverse cardiovascular events (all p<0.05; Table 1) . The number of patients considered by physicians to be a candidate for novel MASH therapy also increased (p<0.05).

CONCLUSIONS

This study demonstrated a substantial clinical and HCRU burden associated with advancing fibrosis, underscoring the need for targeted therapies to prevent further liver damage and associated complications.

ABSTRACT N°27 2/2

Table 1. Clinical Characteristics of patients with F0–F1, F2–F3 and F4 MASH.

	F0–F1	F2–F3	F4	Rho value	p-value
Patient age (years)	**344**	**236**	**7**	0.07	0.0969
Mean±SD	54.7±10.2	55.8±10.2	61.7±7.4		
Patient sex, n (%)	**344**	**236**	**7**		0.5016
Male	204 (59.3)	150 (63.6)	5 (71.4)		
Patient BMI (kg/m^2)	**344**	**236**	**7**	**0.01**	**0.724**
Mean±SD	32.1±4.0	32.3±4.1	29.2±5.5		
Number of blood tests conducted at diagnosis	**334**	**225**	**6**	**0.04**	**0.3133**
Mean±SD	5.2±4.2	5.8±5.0	10.8±7.2		
Number of liver composite tests conducted at diagnosis	**328**	**217**	**6**	**0.3**	**0.4582**
Mean±SD	0.8±0.7	0.9±0.7	0.3±0.5		
Number of imaging scans conducted at diagnosis	**342**	**230**	**7**	**0.18**	**<0.001**
Mean±SD	1.3±0.5	1.5±0.6	1.7±0.8		
Number of blood tests conducted in two years prior to data collection	**251**	**160**	**6**	**0.10**	**0.0481**
Mean±SD	3.0±1.8	3.5±2.3	5.5±3.8		
Number of liver composite tests conducted in two years prior to data collection	**127**	**103**	**3**	**0.02**	**0.9311**
Mean±SD	2.7±2.6	2.9±3.3	1.3±0.6		
Number of imaging scans conducted in 2 years prior to data collection	**259**	**189**	**7**	**0.10**	**0.0279**
Mean±SD	2.2±1.2	2.5±1.6	4.1±3.4		
Top three concomitant conditions at data collection, n (%)	**343**	**236**	**7**		
Dyslipidaemia	201 (58.6)	135 (57.2)	3 (42.9)		**0.6826**
Hypertension	157 (45.8)	135 (57.2)	5 (71.4)		**0.0142**
Type 2 Diabetes	169 (49.3)	115 (48.7)	3 (42.9)		**0.9406**
Physician-reported CV risk, n (%)	**344**	**235**	**7**	**0.28**	**<0.001**
Very low	15 (4.4)	2 (0.9)	0 (0.0)		
Low	167 (48.6)	63 (26.8)	0 (0.0)		
Moderate	111 (32.3)	99 (42.1)	3 (42.9)		
High	35 (10.2)	56 (23.8)	4 (57.1)		
Very high	16 (4.7)	15 (6.4)	0 (0.0)		
Physician reported HCC risk, n (%)	**322**	**221**	**6**	**0.37**	**<0.001**
Very low	32 (9.9)	12 (5.4)	0 (0.0)		
Low	228 (70.8)	90 (40.7)	0 (0.0)		
Moderate	57 (17.7)	103 (46.6)	2 (33.3)		
High	5 (1.6)	15 (6.8)	3 (50.0)		
Very high	0 (0.0)	1 (0.5)	1 (16.7)		
Top three treatments prescribed to treat MASH- associated conditions, n (%)	**342**	**233**	**7**		
Cardiovascular drugs	74 (21.6)	43 (18.5)	1 (14.3)		**0.5994**
GLP-1	42 (12.3)	37 (15.9)	1 (14.3)		**0.4692**
Vitamin E	28 (8.2)	33 (14.2)	2 (28.6)		**0.0244**

Abbreviations: BMI, Body mass index; CV, cardiovascular; HCC, Hepatocellular carcinoma; GLP-1, glucose-like peptide-1; MASH, metabolic-dysfunction associated steatohepatitis; SD, standard deviation

ABSTRACT N°28 1/2

TITLE: REAL-WORLD CLINICAL CHARACTERISTICS AND HEALTHCARE RESOURCE UTILISATION OF PATIENTS WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOHEPATITIS IN FRANCE

AUTHORS

Dr Yestle Kim, Madrigal Pharmaceuticals, West Conshohocken, PA, USA- Presenter
Dr Melinda J Daumont, Madrigal Pharmaceuticals, West Conshohocken, PA, USA
Mr Michele Intorcia, Madrigal Pharmaceuticals, West Conshohocken, PA, USA
Mrs Hayley Wallinger, Adelphi Real World, Bollington, UK
Miss Kathryn Tebbs, Adelphi Real World, Bollington, UK
Miss Rebecca Storm, Adelphi Real World, Bollington, UK
Miss Lena Amari, Adelphi Real World, Bollington, UK
Miss Emily Quiñones, Adelphi Real World, Bollington, UK
Professor Laurent Castera, Department of Hepatology, Beaujon Hospital, Université Paris-Cité, Clichy, France

KEYWORDS

MASH, MASLD, FIBROSIS, HCRU, FRANCE

OBJECTIVES

To describe the clinical characteristics, disease journey and healthcare resource utilisation (HCRU) of patients with metabolic dysfunction-associated steatohepatitis (MASH) in France and assess the need for novel treatments to prevent disease progression.

METHODS

Data were drawn from the Adelphi Real World MASH Disease Specific Programme™, a cross-sectional survey of physicians and their patients with MASH in France from January – May 2024. Physicians provided patient demographics, clinical characteristics and HCRU. Patients were grouped by physician-stated fibrosis severity at data collection (F0–F1, F2–F3 and F4) and were compared using Spearman's Rho and Kruskal-Wallis.

RESULTS

Overall, 74 physicians provided data for 698 patients with MASH (n=240 F0–F1, n=369 F2–F3, n=89 F4). For F0–F1 mean (± standard deviation) age was 54.6±11.1 years, 50.8% were female and mean body mass index was 31.5±6.0kg/m². For F2–F3, this was 56.6±11.4 years, 40.9%, and 32.0±4.8kg/m². For F4 patients, this was 64.9±10.0 years, 41.6% and 33.9±7.6kg/m². Increased fibrosis severity was associated with more symptoms at diagnosis (r=0.12, p<0.01) and data collection (r=0.21, p<0.0001). To assess their MASH, F0–F1, F2–F3, and F4 patients had a mean±SD of 2.0±1.1, 2.3±1.8, 4.0±5.2 liver composite tests (r=0.12, p<0.05), 2.0±1.2, 2.0±1.2, 2.7±1.9 imaging scans (r=0.12, p<0.01) and 3.0±1.8, 3.3±2.6, 5.7±7.1 blood tests in the two years prior to survey. Charlson Comorbidity Index (r=0.82), cardiovascular risk (r=0.25), hepatocellular carcinoma risk (r=0.43) and history of major adverse cardiovascular events increased with fibrosis severity (all p<0.001, Table 1). In the 12 months prior to survey, higher fibrosis severity was associated with more consultations with hepato-gastroenterologists (2.0±1.5, 2.4±1.2, 3.0±2.5 for F0–F1, F2–F3 and F4, respectively, r=0.22, p<0.001), more hospitalisations due to MASH (0.0±0.3, 0.1±0.3, 0.5±1.1, r=0.24), MASH-related comorbidities (0.1±0.3, 0.2±0.6, 0.3±1.0, r=0.10) and more time in hospital (2.7±4.0, 4.1±7.7, 6.7±6.6 nights, r=0.30); all p<0.05. The mean number of prescribed treatments for MASH also increased with fibrosis severity (0.6±1.1, 0.7±1.2, 1.2±1.7 for F0–F1, F2–F3 and F4, respectively, r=0.08, p<0.05).

CONCLUSION

Advancing fibrosis severity was associated with greater clinical and economic burden, underscoring the need for targeted therapies to prevent further liver damage and associated complications.

ABSTRACT N°28 2/2

Table 1. Clinical characteristics of patients with F0–F1, F2–F3 and F4 MASH

	F0–F1	F2–F3	F4	Rho	p-value
Overall, n	**240**	**369**	**89**		
Patient age	**240**	**369**	**89**	**0.23**	**<0.0001**
Mean±SD, years	54.6±11.1	56.6±11.4	64.9±10.0		
Patient sex	**240**	**369**	**89**		**0.0471**
Male, n (%)	118 (49.2)	218 (59.1)	52 (58.4)		
Patient BMI (kg/m²)	**238**	**368**	**88**	**0.11**	**0.0053**
Mean±SD	31.5±6.0	32.0±4.8	33.9±7.6		
Symptoms at diagnosis, n	**232**	**356**	**84**	**0.12**	**0.0014**
Mean±SD	1.3±1.6	1.6±1.9	2.1±2.4		
Top three signs/ symptoms at diagnosis, n (%)	**232**	**356**	**84**		
Fatigue	112(48.3)	175 (49.2)	36 (42.9)		0.5812
Sleep disturbance	53 (22.8)	91 (25.6)	24 (28.6)		0.5476
General weakness	38 (16.4)	64 (18.0)	18 (21.4)		0.5834
Symptoms at data collection, n	**236**	**364**	**88**	**0.21**	**<0.001**
Mean±SD	1.6±1.8	2.2±2.3	3.7±3.4		
Top three signs/ symptoms at data collection, n (%)	**236**	**364**	**88**		
Fatigue	129 (54.7)	215 (59.1)	54 (61.4)		0.4386
Sleep disturbance	66 (28.0)	113 (31.0)	38 (43.2)		0.0309
General weakness	48 (20.3)	90 (24.7)	29 (33.0)		0.06
Top three tests to determine F-stage at diagnosis, n (%)	**212**	**340**	**82**		
VCTE	82 (38.7)	155 (45.6)	49 (59.8)		0.0048
FIB-4	101 (47.6)	120 (35.3)	16 (19.5)		<0.0001
Ultrasonography	65 (30.7)	105 (30.9)	19 (23.2)		0.3707
CCI, n	**230**	**362**	**87**	**0.82**	**<0.0001**
Mean±SD	2.1±0.5	4.3±0.7	4.4±0.9		
Physician perceived CV risk, n (%)	**233**	**355**	**80**	**0.25**	**<0.0001**
Very low	18 (7.7)	6 (1.7)	1 (1.3)		
Low	61 (26.2)	48 (13.5)	9 (11.3)		
Moderate	84 (36.1)	147 (41.4)	23 (28.8)		
High	58 (24.9)	113 (31.8)	28 (35.0)		
Very high	12 (5.2)	41 (11.6)	19 (23.8)		
3-point MACE history, n (%)	**230**	**362**	**87**		**0.0005**
No	225 (97.8)	333 (92.0)	75 (86.2)		
Yes	5 (2.2)	29 (8.0)	12 (13.8)		
Physician reported HCC risk, n (%)	**232**	**348**	**77**	**0.43**	**<0.0001**
Very low	56 (24.1)	38 (10.9)	2 (2.6)		
Low	102 (44.0)	100 (28.7)	10 (13.0)		
Moderate	68 (29.3)	146 (42.0)	15 (19.5)		
High	5 (2.2)	58 (16.7)	38 (49.4)		
Very high	1 (0.4)	6 (1.7)	12 (15.6)		
Whether patient is a candidate for new MASH therapy, n (%)	**240**	**369**	**89**		**0.0007**
Yes	69 (28.8)	155 (42.0)	35 (39.3)		
Undecided	110 (45.8)	156 (42.3)	37 (41.6)		
No	61 (25.4)	58 (15.7)	17 (19.1)		

Abbreviations: SD, standard deviation; FIB-4, fibrosis-4 index; F-stage, fibrosis stage; VCTE, vibration controlled transient elastography; CCI, Charlson Comorbidity Index; CV, cardiovascular; HCC, hepatocellular carcinoma; MACE, major adverse cardiovascular event; MASH, metabolic-dysfunction associated steatohepatitis

ABSTRACT N°29 1/2

TITLE: REAL-WORLD CLINICAL CHARACTERISTICS AND HEALTHCARE RESOURCE UTILISATION OF PATIENTS WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOHEPATITIS IN ITALY.

AUTHORS

Dr Yestle Kim, Madrigal Pharmaceuticals, West Conshohocken, PA, USA- Presenter
Dr Melinda J Daumont, Madrigal Pharmaceuticals, West Conshohocken, PA, USA
Mr Michele Intorcia, Madrigal Pharmaceuticals, West Conshohocken, PA, USA
Mrs Hayley Wallinger, Adelphi Real World, Bollington, UK
Miss Kathryn Tebbs, Adelphi Real World, Bollington, UK
Miss Rebecca Storm, Adelphi Real World, Bollington, UK
Miss Lena Amari, Adelphi Real World, Bollington, UK
Miss Emily Quiñones, Adelphi Real World, Bollington, UK
Professor Luca Miele, Università Cattolica del Sacro Cuore, Rome, Italy and Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

KEYWORDS

MASH, MASLD, FIBROSIS, HCRU, ITALY

OBJECTIVES

To understand the clinical characteristics, disease journey and healthcare resource utilisation (HCRU) of patients with metabolic dysfunction-associated steatohepatitis (MASH) in Italy, and to assess the need for novel treatments to prevent disease progression.

METHODS

Data were drawn from the Adelphi Real World MASH Disease Specific Programme™, a cross-sectional survey of physicians and their patients with MASH in Italy from January – May 2024. Physicians reported patient demographics, clinical characteristics and HCRU. Patients were grouped according to physician stated fibrosis severity at data collection (F0–F1, F2–F3 and F4) and were compared using Spearman's Rho and Kruskal-Wallis.

RESULTS

Overall, 75 physicians reported on 562 patients with MASH (235 were F0–F1, 282 F2–F3 and 45 F4). Mean (± standard deviation) patient age was 55.7±11.1, 56.8±11.7, 66.2±10.2 years, 28.9%, 37.9%, and 47.7% were female, and mean body mass index was 32.5±5.7 kg/m2, 31.8±5.3 kg/m2 and 32.0±5.1 kg/m2, respectively. Increased fibrosis severity was associated with more diagnostic tests (r=0.19), liver composite tests (r=0.12), imaging scans (r=0.20) and blood tests (r=0.11; all $p<0.05$). Increased fibrosis severity was also associated with more symptoms at diagnosis (r=0.19) and at time of data collection (r=0.26) as well as presence of fatigue, general weakness and sleep disturbance at data collection (all $p<0.05$). Charlson Comorbidity Index (r=0.88), perceived cardiovascular risk (r=0.22), and risk of hepatocellular carcinoma (r=0.43) increased with fibrosis severity, as did the requirement for a caregiver (all $p<0.01$; Table 1). In the 12 months prior to data collection, hospitalisations due to MASH (r=0.21) and due to MASH-related comorbidities (r=0.11) increased with fibrosis severity, as did time spent in hospital (r=0.22; all $p<0.05$). Increased fibrosis severity was associated with more treatments prescribed to target MASH-associated comorbidities (r=0.13, $p<0.01$).

CONCLUSION

This study demonstrates the substantial clinical and HCRU burden associated with MASH. The clinical and economic burden associated with advancing fibrosis underscores the urgent need for effective therapeutic strategies to halt progression, prevent liver complications and improve patient outcomes.

ABSTRACT N°29 2/2

Table 1. Clinical Characteristics of patients with F0–F1, F2–F3 and F4 MASH.

	F0–F1	F2–F3	F4	Rho value	p-value
Patient age (years)	**235**	**282**	**45**	**0.15**	**0.0003**
Mean±SD	55.7±11.1	56.8±11.7	66.2±10.2		
Patient sex, n (%)	**235**	**280**	**44**		**0.019**
Male	167 (71.1)	174 (62.1)	23 (52.3)		
Patient BMI (kg/m²)	**235**	**282**	**43**	**-0.08**	0.0502
Mean±SD	32.5±5.7	31.8±5.3	32.0±5.1		
Number of symptoms at diagnosis	**230**	**273**	**44**	**0.19**	**<0.0001**
Mean±SD	1.2±1.8	1.4±1.5)	2.6±2.2		
Number of symptoms at data collection	**232**	**279**	**45**	**0.26**	**<0.0001**
Mean±SD	1.6±2.1	2.2±2.1	4.5±3.4		
Top three signs/ symptoms at data collection, n (%)	**232**	**279**	**45**		
Fatigue	90 (38.8)	133 (47.7)	26 (57.8)		**0.0251**
General weakness	55 (23.7)	85 (30.5)	22 (48.9)		**0.0024**
Sleep disturbance	43 (18.5)	75 (26.9)	18 (40.0)		**0.0038**
Total number of tests conducted at diagnosis	**235**	**281**	**45**	**0.19**	**<0.0001**
Mean±SD	17.8±11.4	22.2±12.2	22.9±12.4		
Number of liver composite tests conducted at diagnosis	**197**	**235**	**34**	**0.12**	**0.0128**
Mean±SD	0.8±0.8	1.0±0.8	1.0±0.8)		
Number of imaging scans conducted at diagnosis	**226**	**276**	**43**	**0.20**	**<0.0001**
Mean±SD	1.3±0.6	1.6±0.7	1.7±0.9		
Number of blood tests conducted at diagnosis	**222**	**264**	**44**	**0.11**	**0.0082**
Mean±SD	7.1±5.5	8.5±5.8	8.3±5.7		
Charlson Comorbidity Index (CCI)	**230**	**263**	**43**	**0.88**	**<0.0001**
Mean±SD)	2.1±0.4	4.3±0.8	4.5±0.9		
Physician-reported CV risk, n (%)	**234**	**280**	**45**	**0.22**	**<0.0001**
Very low	21 (9.0)	9 (3.2)	0 (0.0)		
Low	64 (27.4)	36 (12.9)	1 (2.2)		
Moderate	88 (37.6)	129 (46.1)	27 (60.0)		
High	47 (20.1)	85 (30.4)	16 (35.6)		
Very high	14 (6.0)	21 (7.5)	1 (2.2)		
Physician-reported HCC risk, n (%)	**211**	**271**	**44**	**0.43**	**<0.0001**
Very low	37 (17.5)	14 (5.2)	0 (0.0)		
Low	100 (47.4)	74 (27.3)	3 (6.8)		
Moderate	62 (29.4)	132 (48.7)	16 (36.4)		
High	12 (5.7)	47 (17.3)	17 (38.6)		
Very high	0 (0.0)	4 (1.5)	8 (18.2)		
Does this patient have a caregiver?, n (%)	**231**	**276**	**44**		
Yes	22 (9.5)	66 (23.9)	31 (70.5)		
Number of hospitalisations in the last 12 months due to MASH	**219**	**249**	**43**	**0.21**	**<0.0001**
Mean±SD	0.1±0.2	0.1±0.4	2.1±7.5		
Number of hospitalisations in the last 12 months due to MASH-related comorbidity	**219**	**249**	**38**	**0.11**	**<0.0117**
Mean±SD	0.1±0.3	0.1±0.5	0.4±0.7		
Number of nights spent in hospital (last five hospitalisations)	**31**	**61**	**37**	**0.22**	**0.012**
Mean±SD	2.7±2.4	2.9±3.9	5.6±5.1		
Number of treatments prescribed to control underlying causes of MASH	**225**	**255**	**40**	**0.13**	**0.0033**
Mean±SD	1.8±2.0	2.3±2.0	2.5±2.4		

Abbreviations: BMI, Body mass index; SD, standard deviation; CV, cardiovascular; CCI, Charleson comorbidity index; HCC, hepatocellular carcinoma; MASH, metabolic-dysfunction associated steatohepatitis

ABSTRACT N°30 1/2

TITLE: MECHANISTIC INSIGHTS INTO HEPATIC IRON OVERLOAD IN METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

AUTHORS

Ms. Sahiba Chahal, Research fellow
Mr. Vinesh Sharma, Research fellow
Dr. Vikram Patial, Principal Scientist

KEYWORDS

MASLD, MASH, STEATOSIS, IRON OVERLOAD

OBJECTIVES

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), has been implicated in the dysmetabolic iron overload syndrome (DIOS) and plays a critical role in the progression of MASLD to metabolic dysfunction-associated steatohepatitis (MASH), cirrhosis, and ultimately hepatocellular carcinoma (HCC). The current study aimed to understand and investigate the relation between iron overload and steatosis.

METHODS

In Huh7 cells the effect of hepatic lipid accumulation on iron metabolism was observed by inducing lipid accumulation using a cocktail containing sodium palmitate and sodium oleate. Cell viability assay, intracellular lipid accumulation through Nile Red staining, and triglyceride estimation were done. Expression of genes involved in iron metabolism were examined. Further in-vivo, model was established where Sprague Dawley (SD) rats were subjected to either high fat diet (HFD) or standard chow diet. At the end of the study, changes in body weight, liver weight, serum biochemistry, gene expression and histopathology was done to compare HFD to control group.

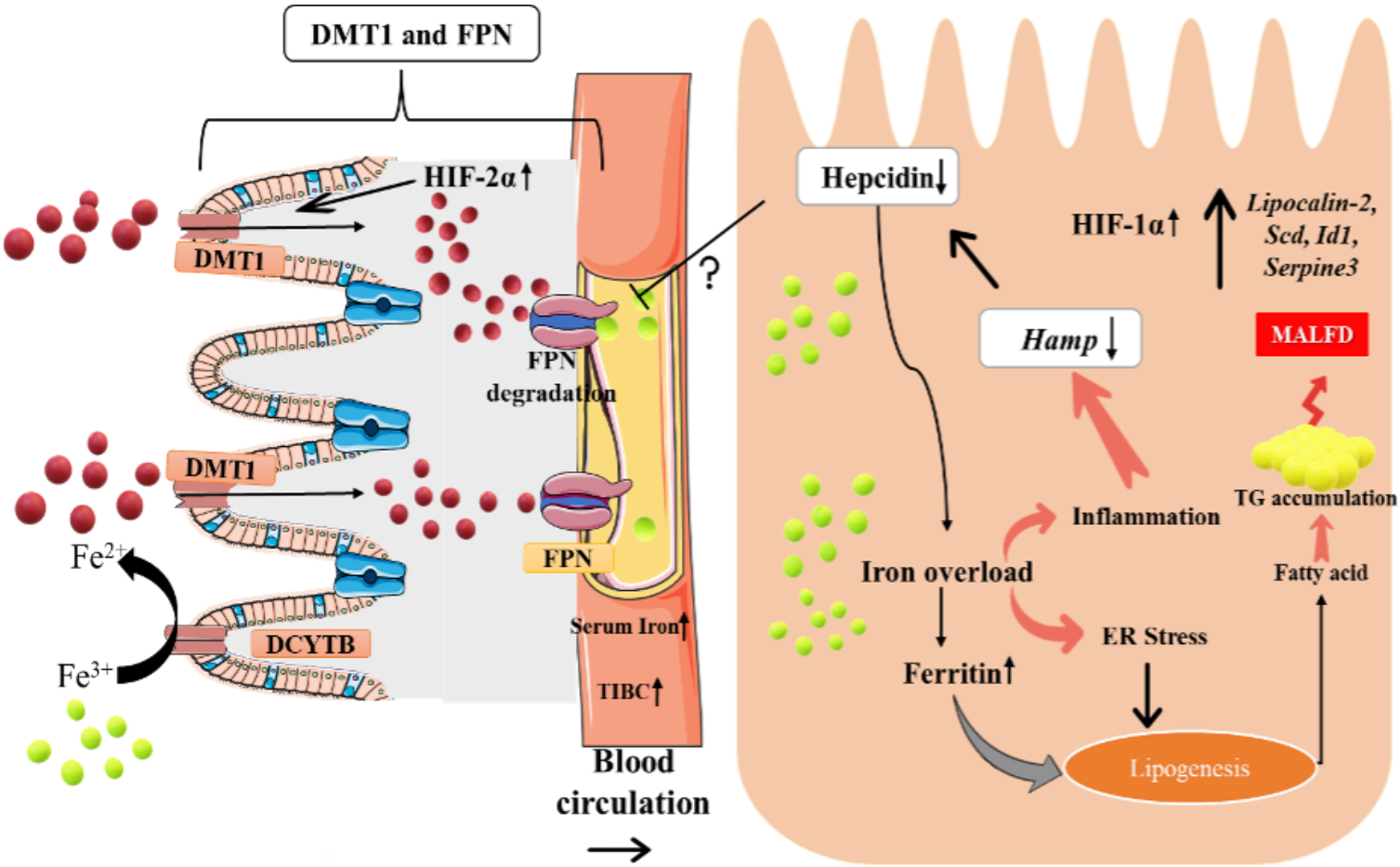
RESULTS

In vitro fatty-acid treatment resulted in decrease in cell viability (%), elevated triglycerides, and lipid accumulation in treated cells as compared to untreated cells. Moreover there were significant changes in gene expression of iron metabolism markers like Transferrin receptor 1 (TFR1), Transferrin (TF), Ferroportin1 (FPN1), and hypoxia inducible factor-2 alpha (HIF-2α) in treated group. In vivo, the HFD fed group had elevated body weight, liver weight, and increased alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and triglycerides in serum indicating liver injury and dyslipidaemia. Additionally, high serum iron, low Total Iron Binding Capacity (TIBC), and hepcidin indicate impaired iron metabolism. Histopathology revealed lipid accumulation and Prussian blue staining showed increased iron deposition in HFD liver tissue. Immunohistochemistry (IHC) revealed increase in Divalent metal transporter (DMT1), Hypoxia Inducible factor-1 alpha (HIF-1α), and HIF-2α in liver and small intestine indicating enhanced compensatory iron uptake. Decreased gene expression of iron markers, hepcidin (Hamp) and Fpn1 and elevated expression of ferritin indicate increased hepatic iron stores. These changes in iron and lipid metabolism are often reflected in MASLD associated iron dysregulation.

CONCLUSIONS

The study revealed that lipid accumulation significantly altered iron metabolism by altering the expression key genes, involved in iron metabolism.

ABSTRACT N°30 2/2



ABSTRACT N°31 1/2

TITLE: RELIABLE MONITORING OF PATIENTS WITH MASLD USING IMAGING: SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

AUTHORS

Michael Ndaa, Perspectum Ltd, Oxford, UK
Cayden Beyer, Perspectum Ltd, Oxford, UK
Dr Anneli Andersson, Perspectum Ltd, Oxford, UK
Prof Walid Ayoub, Karsh Division of Gastroenterology and Hepatology, Department of Medicine, Cedars-Sinai Medical Center, Los Angeles, CA.; Comprehensive Transplant Center, Cedars-Sinai Medical Center, Los Angeles, CA.
Dr Andrea Dennis, Perspectum Ltd, Oxford, UK

KEYWORDS

NITS; SLR; REPEATABILITY; MASLD; IMAGING

OBJECTIVES

As treatments for patients with metabolic dysfunction-associated steatotic liver disease (MASLD) emerge, monitoring of changes in liver health is becoming increasingly important. Reliable detection of treatment response requires quantitative metrics that are sensitive to change and highly repeatable. We systematically reviewed the literature for same-day and different-day repeatability of non-invasive imaging modalities in MASLD.

METHODS

We searched PubMed Central and MEDLINE from 2015 to April 2025 for studies that examined the repeatability of non-invasive image-based technologies in adults with MASLD, specifically MRI iron-corrected T1 (cT1), MRI liver fat content (LFC; also known as proton density fat fraction, PDFF), magnetic resonance elastography (MRE), vibration controlled transient elastography liver stiffness measure (VCTE LSM), controlled attenuation parameter (CAP) and shear wave elastography shear wave speed (SWE-SWS). Two authors independently screened records and extracted data. The within subject standard deviations (wSD), mean and coefficient of variation (CV) were used to calculate the repeatability coefficient (RC) when not directly reported. The absolute (RC) and relative (%RC) for same-day (RCSD) and different-day (RCDD) repeat tests were summarized with a random-effects meta-analysis.

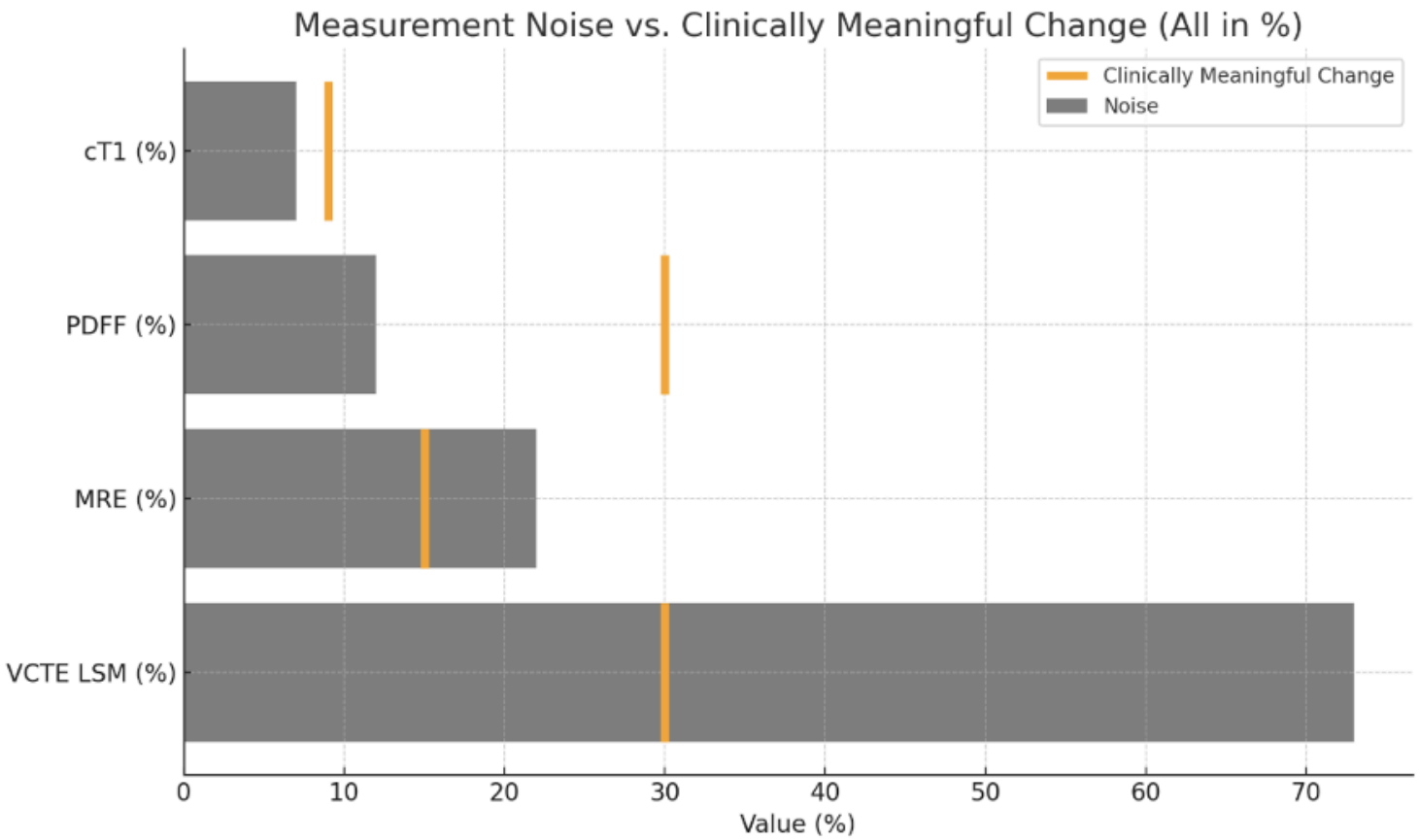
RESULTS

The searches resulted in 19 studies with a total of 1040 individuals. The random-effect average %RCDD was 7% for cT1, 12% for LFC, 22% for MRE, 73% for VCTE LSM, and 26% for CAP, with a median time between repeat scans of 14 days. The range of %RCSD was 4.2% for cT1, 3.6-18% for LFC, 12-22% for MRE, 38-60% for VCTE LSM, 13-37% for CAP and 21% for SWE-SWS. The RCSD and average RCDD for cT1 were 32ms and 65ms. To place these measurement variabilities in the context of monitoring in MASLD, the RCDD can be compared to the established thresholds for clinically significant change for treatment responders: absolute change of 80ms for cT1 and relative reductions of 30% for LFC, 15% for MRE and 30% for VCTE.

CONCLUSIONS

This systematic review and meta-analysis showed that different day repeatability for cT1 and LFC allows detection of change in liver health in people living with MASLD and MASH. The liver stiffness measurements are noisier, and less suited to monitoring individual patients.

ABSTRACT N°31 2/2



ABSTRACT N°32 1/2

TITLE: STATINS AND METFORMIN PRESERVE HEPATIC FUNCTION AND REDUCE PORTAL-SYSTEMIC SHUNTING IN ADVANCED CHRONIC LIVER DISEASE

AUTHORS
Dr. Joanne Imperial, HepQuant, LLC, Denver, CO, USA
Dr. Robert Rahimi, Baylor Scott & White Health, Dallas, TX, USA
Dr. Michael McRae, Custom DX Solutions LLC, Houston, TX, USA
Dr. Gregory Everson, HepQuant, LLC, Denver, CO, USA

KEYWORDS
STATINS; MASH; DIABETES; LIVER FUNCTION

OBJECTIVES In the SHUNT-V study of persons referred for screening or surveillance endoscopy, we used the HepQuant DuO test to evaluate the impact of MASH, diabetes (DM), and maintenance drug therapy on hepatic function and portal-systemic shunting.

METHODS
The 270 subjects for this analysis had either fibrosis stage F3 with platelet count <175,000, compensated cirrhosis, or Child-Pugh B without refractory ascites, refractory encephalopathy or history of variceal hemorrhage. HepQuant DuO tests involved oral administration of d4-cholate and blood sampling at 20 and 60 min. Serum was analyzed for cholate concentrations by LC-MS/MS. A disease severity index (DSI) and portal systemic shunt fraction (SHUNT%) were calculated. Lower DSI indicates better hepatic function; lower SHUNT indicates less portal-systemic shunting. Univariate and multivariate regression tested the association of DSI and SHUNT% with MASH diagnosis, DM diagnosis, and use of diabetic and lipid-lowering drugs.

RESULTS
Subjects were age 61 ± 11 years, body weight 95 ± 23 kg, BMI 34 ± 8, male 52%, White race 91%, and Hispanic ethnicity 16%. Eighty-six percent were overweight, 64% were obese, 48% had MASH, 49% had DM, 47% were taking diabetic drugs, and 41% were taking lipid-lowering drugs, mainly statins. Albumin, bilirubin, INR, alkaline phosphatase, AST, ALT, platelet count, CP score, MELD score, and liver stiffness of MASH subjects were similar to the other subjects. In univariable regression, lower DSI and SHUNT were associated with MASH, DM, diabetic and lipid-lowering drug therapy, metformin, and statins. In multivariable regression analysis of MASH, DM diagnosis, and drug therapy, most of the effect on DSI and SHUNT% was attributable to drug therapy, particularly use of statins (Table 1). When adjusted for all other drug therapies (including GLP-1), only statins and metformin had a significant association with a significant reduction in DSI (Table 2).

CONCLUSION
In the SHUNT-V study of clinically stable but advanced CLD, surprisingly, the diagnosis of MASH or DM was associated with preserved hepatic function and reduced portal-systemic shunting. This association was explained by concomitant use of lipid-lowering and anti-diabetic drug therapy. In contrast to standard assessments, the HepQuant DuO test detected these drug effects.

*This abstract was presented at DDW 2025

ABSTRACT N°33 2/2

Table 1. Multivariable regression analysis of MASH, DM diagnosis, and drug therapy

Impact on DSI (Baseline DSI = 26.2)	**Decline in DSI**	**SE**	**p Value**
Statin	-3.4	1.088	**0.002**
Metformin	-2.7	1.275	**0.036**
DM Diagnosis	-0.6	1.284	0.628
MASH Diagnosis	-0.5	1.072	0.663
Impact on SHUNT% (Baseline SHUNT% = 47.9%)	**Decline in SHUNT%**	**SE**	**p Value**
Statin	-7.5%	0.023	**0.002**
Metformin	-5.1%	0.027	0.066
DM Diagnosis	-2.2%	0.028	0.420
MASH Diagnosis	-3.3%	0.023	0.151

Table 2. Multivariable regression analysis of diabetic and lipid lowering drugs

Impact on DSI (Baseline DSI = 26.2)	**Decline in DSI**	**SE**	**p Value**	**Resultant DSI**	**% Reduction**
Statin	-3.4	1.085	**0.002**	22.8	-12.9%
Metformin	-2.6	1.218	**0.036**	20.3	-22.7%
Glipizide / Glemipiride	-2.0	1.428	0.164	-	-
GLP-1 Analogue	1.3	1.576	0.419	-	-
Pioglitzaone	0.6	2.378	0.813	-	-
SGLT-2 Inhibitor	-1.0	1.629	0.551	-	-
DPP 4 Inhibitor	-1.5	3.067	0.625	-	-
Insulin	-1.0	1.316	0.444	-	-
Vitamin E	-0.9	2.194	0.672	-	-

ABSTRACT N°33 1/2

TITLE: RESMETIROM THERAPY OF MASH-ASSOCIATED CHILD-PUGH A CIRRHOSIS REDUCES ESTIMATED RISK FOR CLINICAL OUTCOME

AUTHORS

Dr. Joanne Imperial, HepQuant, LLC, Denver, CO, USA
Dr. Michael McRae, Custom DX Solutions LLC, Houston, TX, USA
Dr. Rebecca Taub, Madrigal Pharmaceuticals, West Conshohocken, PA, USA
Dr. Gregory Everson, HepQuant, LLC, Denver, CO, USA

KEYWORDS

LIVER FUNCTION; DISEASE SEVERITY INDEX

OBJECTIVES

Resmetirom has been FDA-approved for use in F2/F3 MASH and is under study for use in cirrhosis. The HepQuant DuO test quantifies liver function and physiology from the clearance of orally administered isotopes of cholate. In this study, MAESTRO-NAFLD-1 (NCT04197479), an open label, single arm study of resmetirom in Child Pugh A cirrhosis, we used serial monitoring with DuO to quantify changes in liver function and portal-systemic shunting.

METHODS

The Disease Severity Index (DSI) from DuO was measured in 23 subjects with compensated MASH cirrhosis (eligibility required at least 3 metabolic risk factors, and MASH cirrhosis diagnosed on liver biopsy or according to accepted criteria) at baseline and at 28 (W28) or 48 weeks (W48). For each test, oral deuterium-labelled cholic acid (d4-CA) was administered, blood was sampled at 20 and 60 minutes, serum d4-CA concentrations were measured by LC-MS/MS, and test parameters including DSI were calculated. A Cox proportional hazards regression model (Kittelson et al. 2024) linking DSI to clinical outcome, Risk for Adverse Clinical Event (RISK ACE), was developed from 220 HCV subjects with 52 clinical decompensating events in the HALT-C trial. RISK ACE was evaluated for each of these 23 subjects in MAESTRO-NAFLD-1.

RESULTS

At W48 of resmetirom, 39% of subjects showed improvement from baseline (DSI reduction >2; Chi-square, p=0.046), 44% had stable hepatic function (ΔDSI within ±2), and 17% showed worsening (DSI increase >2). RISK ACE decreased after 48 weeks with resmetirom treatment in 19 of 23 subjects, with a significant reduction in average risk from baseline (−4.0%, p=0.041). Subjects with the greatest hepatic impairment (n=11, baseline DSI >23) showed the greatest reduction in RISK ACE (−7.5%, p=0.053) (Figure).

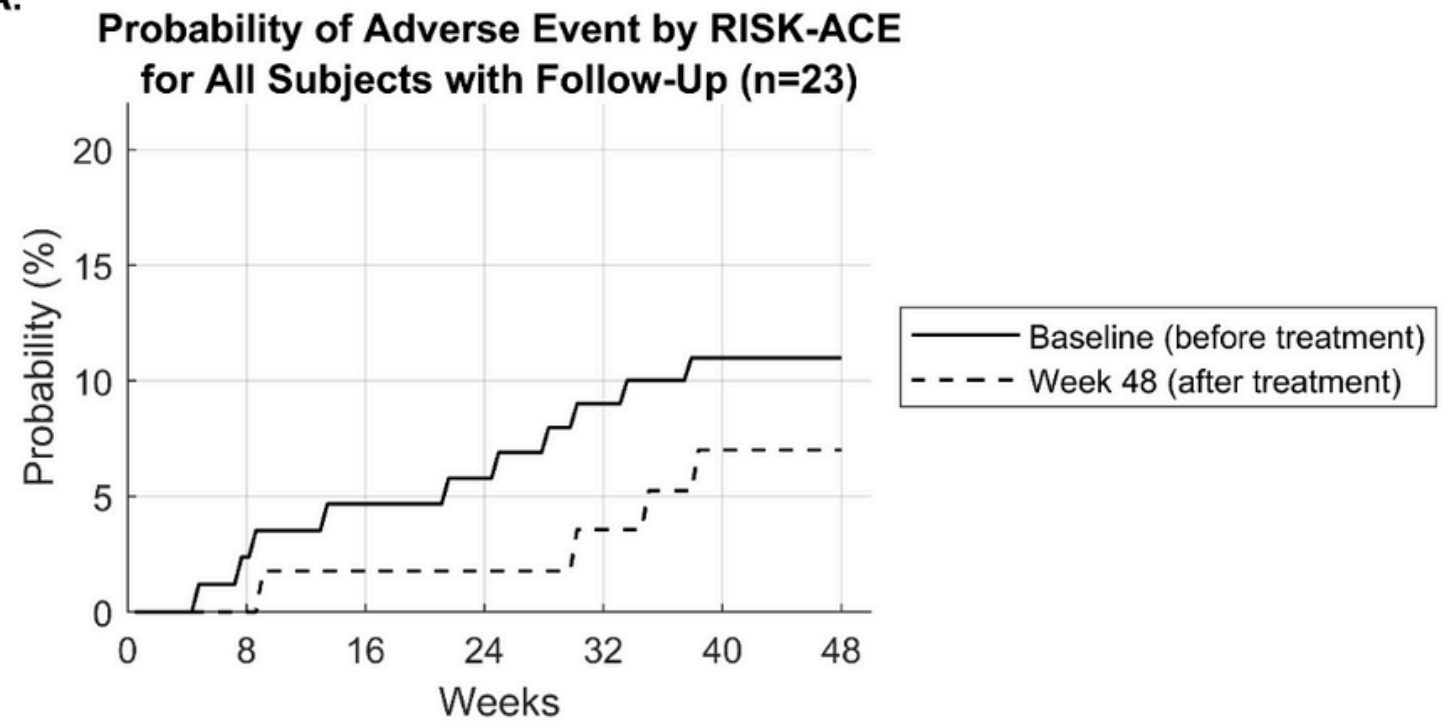
CONCLUSION

Resmetirom therapy of MASH cirrhosis may lower risk for clinical outcome as estimated by RISK ACE from the oral cholate challenge test. Further validation of DuO and Risk ACE is warranted. The results highlight not only a potential positive clinical impact of resmetirom therapy, but also new tools for providing early estimates of clinical benefit in clinical trials.

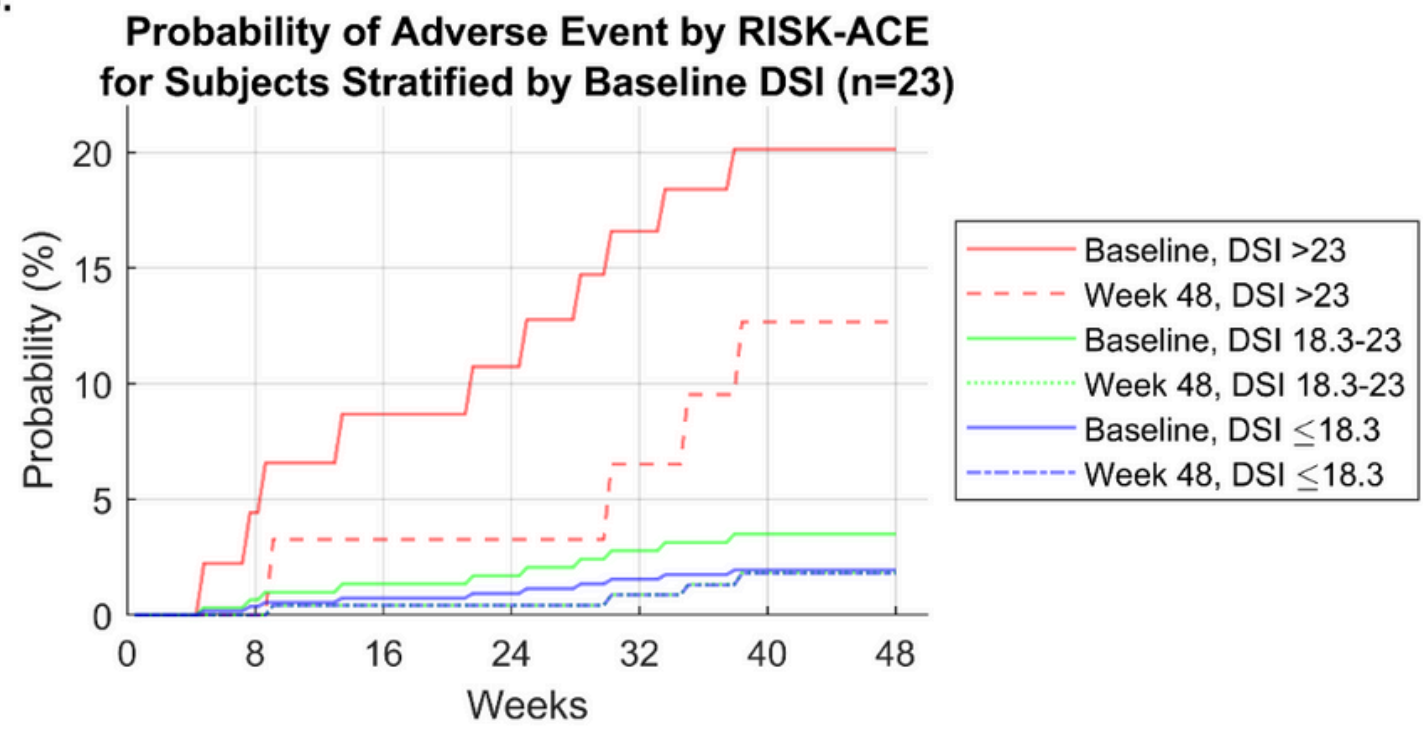
*This abstract was presented at MASH-TAG 2025 and Liver Connect 2025

ABSTRACT N°33 2/2

A.



B.



ABSTRACT N°34 1/2

TITLE: ORAL CHOLATE CHALLENGE TEST DEFINES LIKELIHOOD OF LARGE ESOPHAGEAL VARICES IN OVERWEIGHT AND OBESE POPULATION

AUTHORS

Dr. Joanne Imperial, HepQuant, LLC, Denver, CO, USA
Dr. Michael McRae, Custom DX Solutions LLC, Houston, TX, USA
Dr. Gregory Everson, HepQuant, LLC, Denver, CO, USA

KEYWORDS

MASH; LIVER FUNCTION; LARGE VARICES

OBJECTIVES

The accuracy of transient elastography may be compromised in populations with high prevalence of obesity and MASLD/MASH. In the US-based SHUNT-V study, prevalences of overweight, obesity, and MASLD/MASH were 85%, 65%, and 50%, respectively. In this study, we evaluated the Disease Severity Index (DSI) from the HepQuant DuO test in the diagnostic performance for LEVs.

METHODS

Subjects were enrolled in two prospective studies linking HepQuant test results to endoscopic (EGD) findings. DuO test parameters were quantified from 20- and 60-min concentrations of orally administered d4-cholate (40 mg). The SHUNT-V study enrolled 238 subjects with CP A cirrhosis. We added 217 subjects with prospective HepQuant and EGD data (HALT-C cohort) to expand the sample size and improve estimates of diagnostic performance. We evaluated DSI cutoffs for ruling out LEVs using a minimum acceptable sensitivity of ≥95%. We determined the percentage of subjects who would have avoided EGD and miss rates for LEV among those who avoided EGD. We normalized DSI according to body weight and estimated blood volume.

RESULTS

DSI from DuO was an accurate predictor of LEV across all body sizes. Overall, DSI of 18.3 to rule out LEV had sensitivity 98% (95% CI, 89–100%), would have missed one LEV case (2.0%), and would have prevented 188 unnecessary EGDs (41.3%). AUROCs (95% CI) were comparable across body size groups. For the whole group, DSI normalized by estimated blood volume had the same sensitivity, greater specificity (48% vs. 46%), and would have prevented 7 (1.6%) more EGDs than DSI normalized by body weight. In obese individuals, specificity improved from 31% to 40% when normalizing DSI by blood volume.

CONCLUSION

HepQuant DuO predicts the likelihood of finding LEV on endoscopy in a population characterized by overweight, obesity, and enriched in MASLD/MASH. Normalizing DSI by estimated blood volume may improve the specificity of the test in obese individuals. The simplicity of DuO test administration will likely enhance its implementation by healthcare providers and acceptance by patients. HepQuant DuO may be a useful aid in the decision to avoid or proceed with endoscopic screening or surveillance of LEV.

*This abstract was presented at AASLD 2024, MASH-TAG 2025

ABSTRACT N°34 2/2

Diagnostic performance of DSI for detection of large esophageal varices in normal (BMI<25), overweight (BMI 25-29.9), and obese (BMI >30) subjects in the HALT-C and SHUNT-V studies				
	Normal (n=64)	Overweight (n=145)	Obese (n=246)	All subjects (n=455)
DSI ≤18.3, normalized by body weight				
AUROC	0.84 (0.71-0.95)	0.90 (0.82-0.96)	0.77 (0.69-0.84)	0.82 (0.76-0.86)
Sensitivity	1.00 (0.63-1.00)	1.00 (0.69-1.00)	0.97 (0.83-1.00)	0.98 (0.89-1.00)
Specificity	0.64 (0.50-0.77)	0.62 (0.53-0.70)	0.31 (0.25-0.38)	0.46 (0.41-0.51)
Miss Rate	0 (0.0%)	0 (0.0%)	1 (3.2%)	1 (2.0%)
EGDs Prevented	36 (56.2%)	84 (57.9%)	68 (27.6%)	188 (41.3%)
DSI ≤17, normalized by estimated blood volume				
AUROC	0.85 (0.73-0.95)	0.90 (0.82-0.95)	0.79 (0.70-0.86)	0.83 (0.77-0.88)
Sensitivity	1.00 (0.63-1.00)	1.00 (0.69-1.00)	0.97 (0.83-1.00)	0.98 (0.89-1.00)
Specificity	0.54 (0.40-0.67)	0.59 (0.50-0.67)	0.40 (0.33-0.46)	0.48 (0.43-0.53)
Miss Rate	0 (0.0%)	0 (0.0%)	1 (3.2%)	1 (2.0%)
EGDs Prevented	30 (46.9%)	79 (54.5%)	86 (35.0%)	195 (42.9%)
Values are diagnostic performance (95% CI) or number (%) of subjects				

ABSTRACT N°35 1/2

TITLE: PATHOLOGISTS VALIDATION OF AN AUTOMATED HEPATOCELLULAR BALLOONING DETECTION AI MODEL

AUTHORS

Dr Jack Breen, Perspectum Ltd, Oxford, UK
Dr Dylan Windell, Perspectum Ltd, Oxford, UK
Mr Phil Wakefield, Perspectum Ltd, Oxford, UK
Miss Reema Kainth, Perspectum Ltd, Oxford, UK
Dr Paul Aljabar, Perspectum Ltd, Oxford, UK
Dr Caitlin Langford, Perspectum Ltd, Oxford, UK
Prof Daniela Allende, Cleveland Clinic Foundation, Cleveland, Ohio, USA
Prof Pierre Bedossa, LiverPat, Paris, France
Dr Eve Fryer, Department of Cellular Pathology, John Radcliffe Hospital, OUH NHS FT, Oxford, UK
Prof Timothy Kendall, Institute for Regeneration and Repair, University of Edinburgh, Edinburgh, UK
Prof Robert Goldin, Section for Pathology, Imperial College, London, UK

KEYWORDS

MASLD/MASH, BALLOONING, AI, DIGITAL PATHOLOGY

OBJECTIVES

Hepatocyte ballooning is one of three key histological features in the NAFLD Activity Score (NAS), but is notoriously difficult to assess manually, with low inter-rater reliability. Artificial Intelligence (AI) can automatically detect ballooning hepatocytes and support pathologist assessment, but it remains unclear whether this improves agreement. We report the development of a ballooning detection model, validate automated detection feasibility, and assess both inter-rater and intra-rater reliability among pathologists presented with AI detections.

METHODS

A ballooning hepatocyte detection model was trained using 40 whole slide images (WSIs) from two liver disease trials, with data labelled through a human-in-the-loop approach. This model was applied to 54 further WSIs, from which 216 individual detections were randomly selected for independent review by five pathologists with 14-40+ years of hepatology experience. Three pathologists repeated the process after a 6-week washout to evaluate intra-rater reliability. Pathologists classified ballooning on a cell-based approach using definitions from the expanded ballooning classification (Gill et al., 2023; classic, non-classic or non-ballooning).

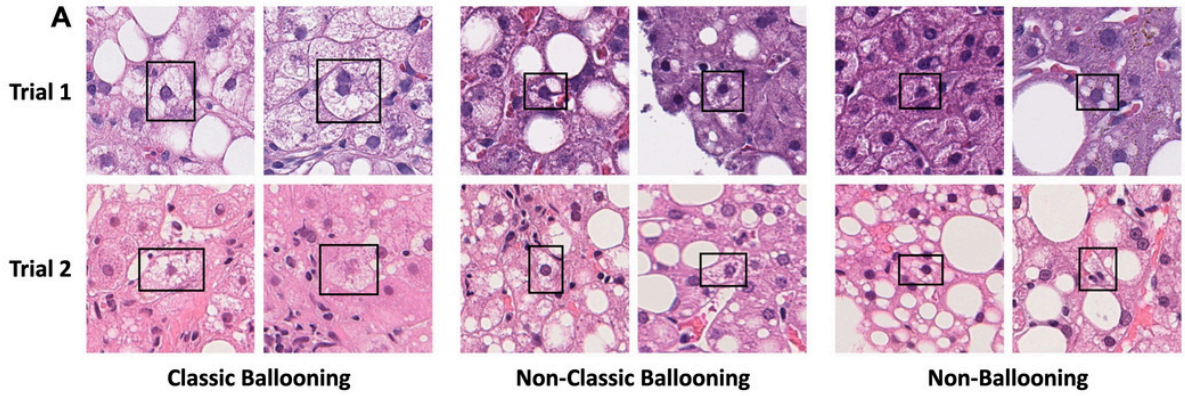
RESULTS

Pairwise agreements on the presence of ballooning ranged from 44-75% (Kappa 0.09-0.43), and when sub-classifying ballooned cells as classic or non-classic, this reduced to 36-70% (Kappa 0.06-0.25). In comparison, three pathologists performing repeated scores had self-agreement rates of 68-81% (Kappa 0.40-0.57) on hepatocyte ballooning, and 62-78% (Kappa 0.36-0.57) when distinguishing classic from non-classic ballooning. The pathologists labelled 13-67% of detections as ballooned hepatocytes, of which 11-71% were labelled as classic ballooned hepatocytes. 81% of detections were labelled as ballooning by at least one pathologist, 61% by at least two, 39% by three, 20% by four, and 6% by all five. The 41 detections all pathologists agreed were not ballooned included eight out-of-focus tissue regions, eleven steatotic hepatocytes, and nine non-hepatocytes (typically sinusoids).

CONCLUSIONS

Scoring and quantifying hepatocyte ballooning can be highly subjective in independent reads. However, in this study, most AI detections were labelled as ballooning by at least one pathologist, indicating that these clinically feasible detections may be useful in guiding pathologists. Further research is required to determine how to utilise AI detections alongside prior reader alignment based on NASH-CRN definitions to improve diagnostic consensus.

ABSTRACT N°35 2/2



B

Percent	Path. 1	Path. 2	Path. 3	Path. 4	Path. 5
Path. 1	100%	71%	61%	62%	68%
Path. 2	63%	100%	54%	61%	74%
Path. 3	41%	46%	100%	74%	43%
Path. 4	51%	51%	44%	100%	49%
Path. 5	66%	70%	36%	41%	100%

Kappa	Path. 1	Path. 2	Path. 3	Path. 4	Path. 5
Path. 1	1.00	0.34	0.30	0.30	0.16
Path. 2	0.25	1.00	0.19	0.28	0.28
Path. 3	0.15	0.19	1.00	0.43	0.09
Path. 4	0.21	0.24	0.20	1.00	0.14
Path. 5	0.14	0.21	0.06	0.06	1.00

Two Classes

Three Classes

Figure 1 – (A) Example AI model detections shown within 100x100 micron regions, grouped by the class assigned by the majority of the five pathologists. (B) Percentage agreement and (Below) Cohen's Kappa agreement scores between five pathologists assessing individual detections. In each table, the upper-right indicates two-class agreement (ballooning vs non-ballooning), lower left indicates three-class agreement (classic ballooning vs non-classic ballooning vs non-ballooning). Kappa scores 0.0-0.2 indicate none-to-slight agreement, 0.2-0.4 indicate fair agreement, and 0.4-0.6 indicate moderate agreement (no scores here reached substantial or near-perfect agreement).

ABSTRACT N°36 1/2

TITLE: AI SYSTEM FOR SPATIAL ANALYSIS OF FIBROSIS IN MASLD AND MASH

AUTHORS

Dr Nazanin Safavian, Perspectum Ltd, Oxford, UK
Dr Alastair Magness, Perspectum Ltd, Oxford, UK
Dr Dylan Windell, Perspectum Ltd, Oxford, UK
Mr Phil Wakefield (Presenter), Perspectum Ltd, Oxford, UK
Miss Reema Kainth, Perspectum Ltd, Oxford, UK
Dr Paul Aljabar, Perspectum Ltd, Oxford, UK
Dr Caitlin Langford, Perspectum Ltd, Oxford, UK
Dr Eve Fryer, Department of Cellular Pathology, John Radcliffe Hospital, OUH NHS FT, Oxford, UK
Prof Timothy Kendall, Institute for Regeneration and Repair, University of Edinburgh, Edinburgh, UK
Dr Ken Fleming, Green Templeton College, University of Oxford, UK
Prof Robert Goldin, Section for Pathology, Imperial College, London, UK

KEYWORDS

MASLD/MASH, CPA, AI, DIGITAL PATHOLOGY

OBJECTIVES

Fibrosis has been quantified in liver histology by measuring collagen proportionate area (CPA) in liver diseases such as Metabolic dysfunction–associated steatotic liver disease (MASLD) and Metabolic dysfunction–associated steatohepatitis (MASH). However, this method can lack spatial context such as bridging and may include non-pathological collagen. To overcome these limitations, we developed an AI system to distinguish pathological and non pathological collagen areas relative to the tissue landmarks of portal tracts and central veins.

METHODS

An AI system was trained to segment key liver tissue components, including parenchyma, bile ducts, hepatic arteries, veins, and connective tissue in Masson’s trichrome stained (MTC) whole slide images (WSIs). Spatial analyses detected anatomical features (portal tracts and central veins) by creating ~100µm equidistant regions around each landmark defined as portal, periportal, pericentral, central, and remaining lobular region (Figure 1a). A second AI model segmented non-pathological collagen, including: Glisson’s capsule, the walls of large vessels and associated connective tissue; distinguish normal connective structures from fibrotic changes (Figure 1b). These models were applied to two independent datasets of patients with MASLD and MASH (N=86, N=22 and N=65 respectively), and quantified fibrosis using three approaches: (1) traditional CPA (%); (2) corrected CPA (%) excluding non-pathological collagen; and (3) regional fibrosis (%) - sum of the fibrosis area in the portal, periportal, and pericentral regions (Figure 1a). Semi-quantitative fibrosis scoring was conducted by one pathologist using the NASH-CRN scoring system and fibrosis measurements compared between each stage (T-test).

RESULTS

Our model identified portal tracts, central veins, and fibrosis in MTC-stained sections (86 WSIs). We measured the periportal fibrosis of 1,114 portal tracts and perivenular fibrosis of 1,050 central veins. The corrected regional fibrosis, corrected CPA, and uncorrected CPA were compared to pathologists’ fibrosis scores (Figure 1c). The Spearman's rho correlations for these three comparisons were 0.71, 0.71, and 0.5, respectively. The Cohen’s d values for these comparisons were 0.9, 0.86, 0.75 for F2 vs F3, and 1.73, 1.4, 1.17 for F3 vs F4, respectively.

CONCLUSIONS

Mapping pathological fibrosis in relation to portal tracts and central veins offers deeper structural insight into the spatial heterogeneity of fibrosis not captured by methods based on slide-level averaging like CPA.

ABSTRACT N°36 2/2

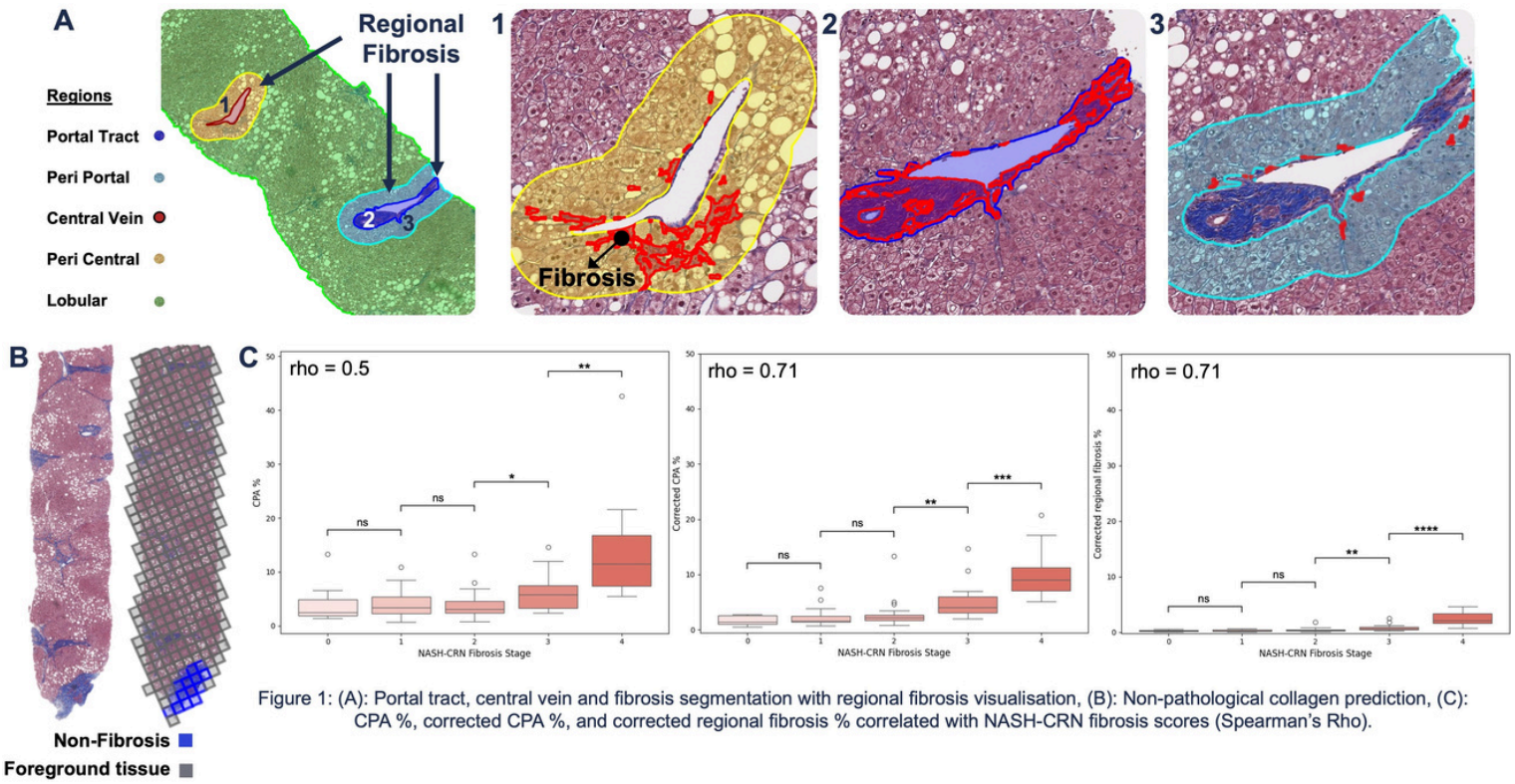


Figure 1: (A): Portal tract, central vein and fibrosis segmentation with regional fibrosis visualisation, (B): Non-pathological collagen prediction, (C): CPA %, corrected CPA %, and corrected regional fibrosis % correlated with NASH-CRN fibrosis scores (Spearman's Rho).

ABSTRACT N°37 1/2

TITLE: PREVALENCE, SEVERITY AND ASSOCIATED FACTORS OF MASLD IN AFRICA: PRELIMINARY RESULTS OF THE MetLive STUDY

AUTHORS

Miss Rumaysa Ahmed, Imperial College London, digestive disease division, St Mary's Hospital London, UK
Mr Bakary Dibba, Medical Research Council Gambia unit at the LSHTM
Mr Ousman Bah, Medical Research Council Gambia unit at the LSHTM
Mr Kitabu Jammeh, Medical Research Council Gambia unit at the LSHTM
Ms Karen Forrest, Medical Research Council Gambia unit at the LSHTM
Ms Anna Sessa, Imperial College London, digestive disease division, St Mary's Hospital London, UK
Mr Erwan Vo Quang, Medical Research Council Gambia unit at the LSHTM
Mr Ben Mullish, Imperial College London, digestive disease division, St Mary's Hospital London, UK
Ms Isabel Garcia Perez, Imperial College London, digestive disease division, St Mary's Hospital London, UK
Mr Umberto D'Alessandro, Imperial College London, digestive disease division, St Mary's Hospital London, UK
Ms Isabel Bough, University of Cape Town, South Africa
Mr Mark Sonderup, University of Cape Town, South Africa
Mr Yusuke Shimakawa, Unité d'Epidémiologie des Maladies Emergentes, Pasteur Institute Paris, France
Mr Gibril Ndow, Medical Research Council Gambia unit at the LSHTM
Prof Maud Lemoine, Imperial College London, digestive disease division, St Mary's Hospital London, UK

KEYWORDS

MASLD, T2DM, WAIST CIRCUMFERENCE, HYPERTENSION

OBJECTIVES

Metabolic dysfunction-associated steatotic liver disease (MASLD) remains a neglected public health issue in the WHO African region, despite the rising prevalence of obesity and diabetes. To fill the knowledge gap on MASLD in Africa, we established the MetLive cohort study of individuals with metabolic disorders in The Gambia (West Africa) and South Africa, aiming to assess the prevalence, risk factors and clinical outcomes of MASLD within these populations.

METHODS

Consecutive patients with obesity, hypertension (HTN) or type 2 diabetes mellitus (T2DM) were recruited in both The Gambia and South Africa. Here, we present a preliminary cross-sectional analysis of patients enrolled prospectively in The Gambia. Each participant had anthropometric measurements, socio-economic, diet and lifestyle questionnaires alongside collection of blood, urine and rectal/saliva swabs. Fasting glucose, lipid and liver tests were measured along with assessment of hepatic steatosis and liver stiffness (LSM) using FibroScan. MASLD was defined as CAP≥248 dB/m (or hyperechoic liver in case of invalid CAP measurements), advanced liver fibrosis as LSM≥8 kPa, and cirrhosis as LSM≥12 kPa.

RESULTS

Between 11th April 2025 and 12th June 2025, 179 consecutive patients were enrolled and analysed. Among these participants, the median age was 50 years (45-62), mainly female (79%), with T2DM (75%). MASLD was present in 64/179 participants (36%), of which 14% had advanced fibrosis, with one case of cirrhosis. HBV prevalence was similar between patients with or without fibrosis. Multivariable analysis revealed waist circumference (WC) (OR:1.09; 95% CI: 1.02-1.19; p=0.0187) and HTN (OR:2.67; 95% CI: 1.05-6.00; p=0.0405) to be independent factors associated with MASLD. Using the CAP method as a reference, combined parameters (WC and HTN) demonstrative good predictive ability for significant steatosis (AUROC: 0.81; 95% CI: 0.71-0.89; p<0.0001).

ABSTRACT N°37 2/2

CONCLUSIONS

In The Gambia, approximately 40% of patients with metabolic disorders have MASLD, a prevalence slightly lower than global estimates. Our findings suggest that the measurements of WC and HTN could be used as simple low-cost screening tools for MASLD, particularly in resource-limited settings. These findings will be further validated with additional data from The Gambia and South Africa.

ABSTRACT N°38

TITLE: ASSESSING THE CLINICAL CHARACTERISTICS AND OUTCOMES OF PATIENTS PRESCRIBED RESMETIROM IN A REAL-WORLD EHR DATABASE

AUTHORS

Dr. Sammy Saab, Pfleger Liver Institute, Los Angeles, CA, USA
Dr. Yestle Kim, Madrigal Pharmaceuticals, Inc.., West Conshohocken, PA, USA
Mr. Dave Lewandowski, Veradigm, Chicago, IL, USA
Dr. Jessamine Winer-Jones, Veradigm, Chicago, IL, USA
Ms. Maryam Ajose, Veradigm, Chicago, IL, USA
Dr. Machaon Bonafede, Veradigm, Chicago, IL, USA
Dr. John O'Donnell, Madrigal Pharmaceuticals, Inc.., West Conshohocken, PA, USA
Mrs. Taylor Ryan, Veradigm, Chicago, IL, USA

KEYWORDS

MASH, REAL-WORLD DATA, RESEMETIROM

OBJECTIVES

To describe the real-world clinical characteristics and clinical outcomes among adults with noncirrhotic MASH initiating resmetirom in the US.

METHODS

This retrospective study used the Veradigm Network EHR linked to claims to identify patients (18+) with ≥1 pharmacy record (earliest=index date) for resmetirom between 03/14/2024-04/30/2025. Patients with missing age or sex and evidence of end stage liver disease (cirrhosis, decompensated cirrhosis or lactulose treatment, other ascites, hepatic encephalopathy, unspecified encephalopathy, liver transplant, hepatocellular carcinoma) pre-index were excluded. Demographics, comorbidities, and index prescription strength were described at baseline. Fibrosis staging and liver enzyme levels were evaluated at baseline and post-resmetirom initiation (follow-up), upon data availability. Concomitant GLP-1 receptor agonist (RA) use, and resmetirom treatment duration were assessed during the 6-month follow-up period.

RESULTS

Of the 1,690 patients initiating resmetirom, 394 were eligible for the analysis. Mean (SD) age was 58.6 (13.0) years, majority were female (59.9%), and White (71.6%). At baseline, 72.3% of patients had obesity, and almost half of the cohort had type 2 diabetes mellitus (48.0%), hyperlipidemia (48.0%), and/or hypertension (47.7%). At index, most patients were prescribed resmetirom 80 mg (50.0%) or 100 mg (44.4%) dose. Concomitant use with GLP-1 RAs during the follow-up period was seen in about one-third of patients (30.2%), of which 80 patients (67.2%) had baseline GLP-1 RA use. Between baseline and follow-up, the mean liver enzyme levels decreased in alanine transaminase (63.3 U/L to 53.7 U/L; n=203), aspartate transaminase (47.6 U/L to 41.3 U/L; n=198), low-density lipoprotein cholesterol (92.9 mg/dL to 83.7 mg/dL; n=80), and triglycerides (181.0 mg/dL to 153.0 mg/dL; n=81). Mean liver stiffness measured by vibration-controlled transient elastography (VCTE) was 11.5 kPa (n=19) in baseline and 9.5 kPa (n=10) in follow-up. No changes in body mass index were observed.

CONCLUSIONS

In this descriptive real-world analysis, patients who initiated resmetirom had observed mean decreases in liver enzyme levels and reductions in mean VCTE results after approximately 6 months of follow-up. Additional assessment with longer follow-up is required to better understand the real-world long-term effectiveness of resmetirom among patients with MASH.

ABSTRACT N°39

TITLE: THE NATURAL HISTORY AND ECONOMIC BURDEN OF METABOLIC DYSFUNCTION-ASSOCIATED STEATOHEPATITIS IN THE US REAL-WORLD SETTING

AUTHORS

Dr. Yestle Kim, Madrigal Pharmaceuticals, Inc., West Conshohocken, PA, USA
Dr. Ni Zeng, Veradigm, Chicago, IL, USA
Dr. Jessamine Winer-Jones, Veradigm, Chicago, IL, USA
Ms. Maryam Ajose, Veradigm, Chicago, IL, USA
Dr. Machaon Bonafede, Veradigm, Chicago, IL, USA
Dr. John O'Donnell, Madrigal Pharmaceuticals, Inc.., West Conshohocken, PA, USA
Mrs. Taylor Ryan, Veradigm, Chicago, IL, USA

KEYWORDS

MASH, NATURAL HISTORY, REAL-WORLD DATA

OBJECTIVES

To describe the clinical characteristics and economic burden of metabolic dysfunction-associated steatohepatitis (MASH) patients, stratified by evidence of baseline end stage liver disease (ESLD) and to assess the progression to ESLD.

METHODS

The Veradigm Network EHR linked to claims was used to identify adults (18+) with ≥1 inpatient claim or ≥2 outpatient claims/records with a MASH diagnosis (ICD-10-CM: K75.81) between 07/01/2019-04/30/2025 (earliest diagnosis=index). Inclusion criteria included: no missing age or sex, continuous enrollment ≥2 years pre-index (including the index) (baseline) and ≥1 year post-index (follow-up), and no evidence of resmetirom initiation or other causes of liver disease (e.g., viral hepatitis) during the study period. Patients were stratified by evidence of baseline (up to 30 days post-index) ESLD (cirrhosis, decompensated cirrhosis or lactulose treatment, other ascites, hepatic encephalopathy, unspecified encephalopathy, liver transplant, hepatocellular carcinoma). Patient characteristics, including non-invasive tests (NITs) where available, are described at baseline. In follow-up, progression to advanced liver events and total all-cause per-patient-per-year (PPPY) healthcare costs were described.

RESULTS

A total of 68,209 MASH patients (mean [SD] age: 55.1 [14.0] years, BMI ≥30.0 kg/m2: 71.6%) were followed for average 2.8 (1.3) years; 19,741 patients had baseline ESLD. Baseline NITs were more common in those with baseline ESLD vs. without: abdominal ultrasound (63.8% vs. 49.3%), computed tomography (56.4% vs. 27.2%), and MRI (14.8% vs. 5.2%). Among 48,468 patients without baseline ESLD, 15.2% progressed, most often to decompensated cirrhotic events (n=5,935, 12.3%) or cirrhosis (n=2,803, 5.8%) within 18.8 (14.5) and 16.9 (14.3) months, respectively. Mean (SD) PPPY costs were higher among patients with baseline ESLD ($79,833 [$470,608]) than without ($27,267 [$98,384]). In patients without baseline ESLD, those who progressed had higher PPPY costs ($57,132 [$208,634] vs. $21,914 [$58,520]). Among 683 patients with the highest costs (top 1%), 467 (68.4%) had baseline ESLD and 123 (18.0%) did not but progressed during follow-up.

CONCLUSIONS

While patients without baseline ESLD had lower PPPY healthcare costs, those who later progressed incurred 2.6x costs than those who did not, highlighting the need for better identification and treatment options to slow disease progression and reduce the economic burden.

ABSTRACT N°40

TITLE: RELATIONSHIP BETWEEN NON-INVASIVE TESTS, CLINICAL OUTCOMES AND LIVER BIOPSY AMONG REAL-WORLD MASH PATIENTS

AUTHORS

Dr. Arun Sanyal, Virginia Commonwealth University School of Medicine
Dr. Sid Barritt, University of North Carolina School of Medicine
Dr. Yestle Kim, Madrigal Pharmaceuticals
Dr. John O'Donnell, Madrigal Pharmaceuticals
Dr. Breda Munoz, Target RWE
Dr. Feng Yu, Target RWE
Dr. Andrea Mospan, Target RWE
Dr. Heather Morris, Target RWE
Dr. Vincent Wai-Sun Wong, Chinese University of Hong Kong
Dr. Michael Roden, Heinrich Heine University Düsseldorf, Düsseldorf, Germany

KEYWORDS

MASH, REAL-WORLD, BIOPSY, NON-INVASIVE TESTS

OBJECTIVES

Liver biopsy is the reference standard for assessing disease severity in metabolic dysfunction-associated steatohepatitis (MASH), yet biopsies are rare in clinical practice. Given that non-invasive tests (NITs) are reasonable surrogates for assessing disease severity, this analysis utilized NITs and fibrosis stage from liver biopsy and assessed clinical outcomes.

METHODS

This analysis included US adults in TARGET-NASH, a longitudinal observational study. Eligible participants had one liver biopsy and two FIB-4 measurements. Participants were classified into two subgroups based on longitudinal changes in FIB-4 category (<1.3, 1.3-2.67, >2.67) between the first and second assessment: stable/improved (no change/decrease in FIB-4 category) or worsened (increase in FIB-4 category). Fine-Gray multivariable subdistribution hazard models with time-varying covariates assessed the association between FIB-4 and time to clinical events.

RESULTS

The analysis cohort (n=625) had a median age of 56, with 74% identifying as non-Hispanic White, 67% female, a median BMI of 33kg/m2, and 14.2% (n=89) and 85.8% (n=536) were classified in the worsened and stable/improved subgroups, respectively. The mean (SD) of first FIB-4 for each FIB-4 category was: 0.85 (0.26), n=227 for FIB-4<1.3; 1.92 (0.40), n=230 for FIB-4=1.3-2.67; and 4.90 (2.43), n=168 for FIB-4 >2.67. The worsened group had a higher incidence of cirrhosis (25.6%, incidence rate = 5.4 per 100 person-years) compared with the improved/stable group (p=0.044). Among those with non-cirrhotic MASH, a higher proportion experienced a composite of clinical events in the worsened group (44.8%) than the improved/stable group (24.5%, p=0.021). Participants with FIB-4 >2.67 had a higher risk of all-cause mortality (HR:6.02, 95% CI: 2.86-12.68), and 5.5 times the risk of progressing to cirrhosis (HR: 5.48, 95% CI:2.39-12.57) compared with those having FIB-4 <1.3.

CONCLUSIONS

Given the limitations of biopsy NITs like FIB-4 may be used to assess disease severity and disease progression. Changes in FIB-4 category were associated with differences in cirrhosis risk and clinical outcomes. These findings reinforce the potential role of FIB-4 as a non-invasive tool for risk assessment in MASH management.

ABSTRACT N°41 1/2

TITLE: PREVALENCE AND RISK FACTORS OF FIBROSIS IN A REAL-WORLD COHORT: DATA FROM THE GERMAN SLD-REGISTRY

AUTHORS

Dr. Maurice Michel, Department of Internal Medicine II at the Saarland University Medical Center, Homburg, Germany
Prof. Dr. Andreas Geier, Division of Infectious Diseases, Department of Internal Medicine II, University of Würzburg Medical Center, Würzburg, Germany
Prof. Dr. Stefan Zeuzem, Goethe University Hospital, Frankfurt, Germany
Dr. Manfred von der Ohe, Gastroenterologische Studiengesellschaft Herne, Herne, Germany
Prof. Dr. Münevver Demir, Department of Hepatology and Gastroenterology, Campus Virchow-Klinikum and Campus Charité Mitte, Charité - Universitätsmedizin Berlin, Berlin, Germany
Dr. Renate Heyne, Leberzentrum Checkpoint, Berlin, Germany
Dr. Stephan Grunwald, Zentrum für Infektiologie Berlin/Prenzlauer Berg, Berlin, Germany
Prof. Dr. Jens U. Marquardt, Department of Medicine I, University Hospital Schleswig-Holstein, Lübeck, Germany
Yestle Kim, Madrigal Pharmaceuticals, Inc., West Conshohocken, Pennsylvania, USA
Dr. Hardo Fischer, Madrigal Pharmaceuticals GmbH, Vienna, Austria
Melinda Daumont, Madrigal Pharmaceuticals GmbH, Zug, Switzerland
Prof. Dr. Thomas Berg, Division of Hepatology, Department of Medicine II, Leipzig University Medical Center, Leipzig, Germany
Prof. Dr. Elke Roeb, Department of Gastroenterology, Medical Clinic II, Justus Liebig University, Giessen, Germany
Prof. Dr. Wolf Peter Hofmann, Gastroenterologie am Bayerischen Platz, Berlin, Germany; Leberstiftungs-GmbH Deutschland, Hannover, Germany
Prof. Dr. Jörn M. Schattenberg, Department of Internal Medicine II at the Saarland University Medical Center, Homburg, Germany

KEYWORDS

MASLD; METABOLIC RISK FACTORS; VCTE

OBJECTIVES

Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common chronic liver disease in Germany. Liver fibrosis associated with MASH, the inflammatory form of MASLD, is associated with worse outcomes and increased mortality. Non-invasive diagnostics are used to identify patients at risk who may benefit from pharmacological treatment to prevent progression to cirrhosis (F4). This analysis describes the prevalence and risk factors of fibrosis related to MASLD in Germany.

METHODS

The German SLD-Registry is a prospective, non-interventional registry study recruited in secondary and tertiary care. The cohort included 1,508 patients at baseline followed up to 3 years. Fibrosis was assessed by liver stiffness measurement (kPa) using vibration-controlled transient elastography (VCTE) and categorized in strata: 8.5–12 kPa (F2), >12–15 kPa (F3), and >15 kPa (F4). A subgroup analysis (n=360) was conducted in patients with baseline VCTE 8.50-<15 kPa or VCTE ≥15-20 kPa and platelets ≥140 x109/L representing a non-cirrhotic MASH population. Demographic and clinical characteristics, as well as cardiometabolic risk factors were analyzed.

ABSTRACT N°41 2/2

RESULTS

The overall study cohort (n=1,508) included 50% males and 63% were obese (BMI>30). The prevalence of F2, F3, and F4 fibrosis was 49% (n=227), 17% (n=80), and 34% (n=161), respectively. In the presumed non-cirrhotic MASH sub-cohort (n=360), 47% were male, mean age of 54 (±12.9) years and mean BMI of 36 (±9.3) kg/m²; 72% were obese. Type 2 diabetes (T2D) was present in 53%, and 58% had ≥3 cardiometabolic risk factors, rising to 86% among those with T2D (p<0.001). 94% had platelets ≥140x109/L. In the sub-cohort, F2, F3, and F4 fibrosis were found in 65%, 23%, and 13%, respectively. The F3 (25%) and F4 (18.8%) category was more prevalent in patients with T2D compared to those without (p<0.001). After 3 years, fibrosis progression from F2 to F3 occurred in 20% (4/20) and from F3 to F4 in 50% (10/20) of cases with available data.

CONCLUSIONS

Patients with MASLD in Germany show a high prevalence of fibrosis and associated cardiometabolic risk factors. Identifying those with fibrosis may help guide future treatment options to improve outcomes.

ABSTRACT N°42 1/2

TITLE: "WHICH DOOR"? PERSONALIZED PATHWAY IN MASLD RISK STRATIFICATION TO REDUCE RISK OF FUTURE CLINICAL EVENTS

AUTHORS

Dr Anneli Andersson, Perspectum
Dr Edward Jackson, Perspectum
Dr Prashant Pandya, Perspectum
Dr Andrea Dennis, Perspectum

KEYWORDS

MASH, OUTCOMES, CT1

OBJECTIVES

Metabolic dysfunction-associated steatotic liver disease (MASLD) is the leading cause of liver disease, affecting 1/3 of the global population. Clinical guidelines for MASLD focus on fibrosis assessment (incl. FIB-4) based on risk of liver related events (LRE), but patients with MASLD are also at risk of renal disease, extrahepatic cancers, new onset of diabetes and cardiovascular related outcomes. In a retrospective analysis of data from the UK biobank (UKB), we examined potential personalized risk stratification by adding iron-corrected T1 (cT1), an MRI-derived biomarker of liver health shown to be elevated in 58% of MASLD cases with low FIB-4, to improve the MASLD pathway.

METHODS

Between 2016 and 2020, 100,000 community-based individuals from the original UKB study (baseline) were invited for multi-parametric MRI as part of the UKB imaging sub-study (follow-up). FIB-4 data was available at baseline and the imaging was performed an average of 10 years later. Clinical events data was collected post the imaging visit and associations with FIB-4 and cT1 examined using cox proportional models. cT1 clinical thresholds were ≥800ms (moderately elevated) and ≥875ms (high); FIB-4 thresholds were ≥1.3 (adjusted to 2 in those over 60 years; intermediate) and ≥2.67 (elevated).

RESULTS

In a cohort of 38,800 participants (mean age 68, 60% male, mean BMI 28, 15% T2D, mean follow-up time, 3.8 years), risk of LRE was associated with elevated FIB-4 (figure 1), while low or intermediate FIB-4 carried no risk of LRE unless cT1 was elevated. The greatest risk was in those with both FIB-4 ≥ 2.67 and cT1 ≥ 875ms (liver hospitalisation HR: 53 [7, 380]; LRE HR: 470 [62, 3633]). Low FIB-4 with moderately elevated cT1 was associated with CV hospitalisation (HR: 1.3 [1,1.7]) and those with intermediate FIB-4 at baseline but high cT1 at the imaging visit were at significant risk of new onset diabetes (HR 4.9 [1.8, 13.4]) and CKD (HR: 5.1 [1.8, 13.8]).

CONCLUSIONS

Liver health risk stratification significantly improves when adding cT1 to the current fibrosis-only diagnostic pathway for MASLD, better informing through which onwards specialist or “door” the patient should progress to reduce the likelihood of experiencing a future clinical event.

ABSTRACT N°42 2/2

Figure 1: New onset clinical events following the imaging visit. Hazard ratios (adjusted for age, sex and BMI) for future clinical event by FIB-4 and cT1 thresholds. NB: In those over 60 years old, the lower FIB-4 threshold was adjusted from <1.3 to <2.0.

ABSTRACT N°43 1/3

TITLE: REAL-WORLD SAROGLITAZAR IMPACT ON FIBROSCAN, TRANSAMINASES, AND CAP IN MASH: SINGLE-CENTER STUDY

AUTHORS
DR. MOHAN PRASAD V. G., VGM HOSPITAL, COIMBATORE, INDIA
DR. MITHRA PRASAD, VGM HOSPITAL, COIMBATORE, INDIA
DR. MADHURA PRASAD SUMAN, VGM HOSPITAL, COIMBATORE, INDIA
DR. VAMSI MURTHY K, VGM HOSPITAL, COIMBATORE, INDIA
DR. JACKSON KEEFER JERRY, VGM HOSPITAL, COIMBATORE, INDIA
DR. CINSIA THARUMIA JAGADEESAN, VGM HOSPITAL, COIMBATORE, INDIA

KEYWORDS
SAROGLITAZAR, FIBROSCAN, MASH, CAP, LIVERSTIFFNESS

OBJECTIVES
This study aimed to evaluate the real-world efficacy of Saroglitazar, a dual peroxisome proliferator-activated receptor (PPAR) α/γ agonist, in improving liver stiffness, hepatic steatosis, transaminase levels, and body mass index (BMI) in patients with metabolic dysfunction-associated steatohepatitis (MASH), using FibroScan and biochemical markers.

METHODS
A prospective observational study was conducted at a single tertiary center involving 416 patients (320 males [77%], 96 females [23%]) with a mean age of 51.23 ± 12.15 years (range 17–84). Patients underwent baseline and follow-up assessments after initiating Saroglitazar, including BMI, serum aspartate aminotransferase (AST/SGOT), alanine aminotransferase (ALT/SGPT), controlled attenuation parameter (CAP), and liver stiffness (kPa) via transient elastography (FibroScan). FibroScan-based fibrosis grading (Grades I–IV) was recorded. Paired t-tests and Pearson correlations were used; $p < 0.05$ was considered statistically significant.

RESULTS
Mean SGOT decreased from 54.48 ± 67.27 to 41.15 ± 46.72 IU/L ($p < 0.05$), and SGPT from 54.49 ± 65.49 to 37.38 ± 56.27 IU/L ($p < 0.001$). CAP improved significantly from 268.63 ± 42.87 to 253.43 ± 47.19 dB/m ($p < 0.001$). BMI showed a non-significant reduction from 28.75 ± 5.06 to 28.45 ± 5.13 kg/m² ($p > 0.05$), and liver stiffness changed from 13.70 ± 21.03 to 13.89 ± 26.58 kPa ($p > 0.05$). No significant correlations were observed between CAP and BMI, SGOT, SGPT, or kPa.

FibroScan subgroup analysis showed decreases in all grades:
Grade I (n=8): 5.29 ± 0.95 to 5.23 ± 1.68 (↓1%)
Grade II (n=96): 9.46 ± 0.9 to 8.0 ± 1.09 (↓15%)
Grade III (n=111): 16.62 ± 0.84 to 10.11 ± 7.69 (↓13%)
Grade IV (n=32): 39.61 ± 2.49 to 30.26 ± 23.03 (↓24%)
No patients showed fibrosis progression.

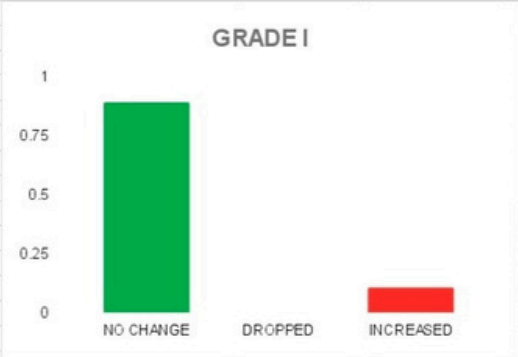
CONCLUSIONS
Saroglitazar was associated with significant reductions in liver enzymes and steatosis (CAP) in MASH patients. Although changes in BMI and liver stiffness were not significant, subgroup analysis indicated fibrosis regression across all stages, most notably in Grade IV. Further histology-based validation is warranted.

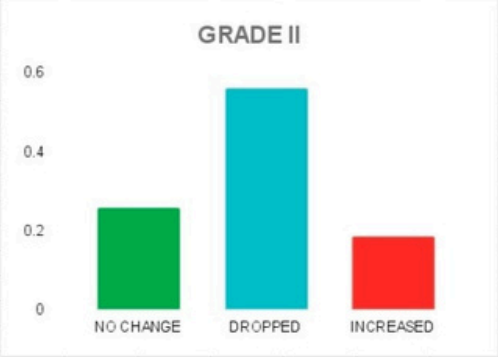
ABSTRACT N°43 2/3

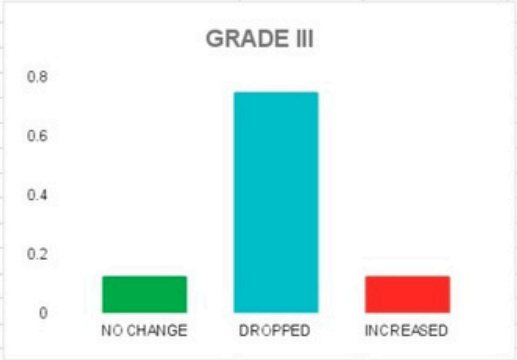
ASSOCIATION OF FIBRO SCAN WITH GRADES BASELINE VS FOLLOWUP

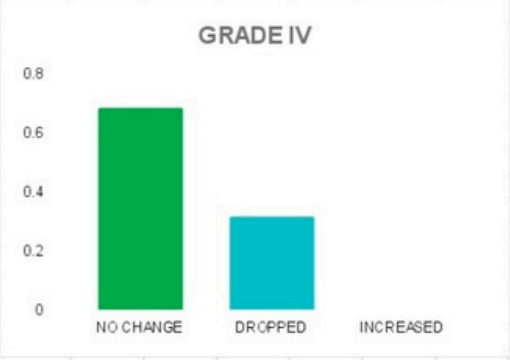
	FIBROSCAN BASELINE VS FOLLOWUP		
FIBRO SCAN GRADE	NO CHANGE	DROPPED	INCREASED
I	89%		11%
II	26%	56%	19%
III	13%	75%	13%
IV	68%	32%	

P<0.001



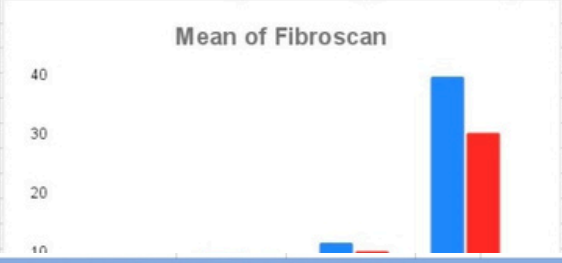






MEAN OF FIBROSCAN

FIBRO SCAN GRADE	BASELINE	FOLLOWUP	Mean Dropped
GRADE I (n=83)	5.29+/- 0.95	5.23 +/- 1.68	1%
GRADE II (n=43)	9.46+/-0.9	8.0+/-10.93	15%
GRADE III (n=17)	11.62+/-0.84	10.11+/-7.69	13%
GRADE IV (n=41)	39.61+/-22.89	30.26+/-23.03	24%



MEAN OF ASSOCIATIVE VARIABLES WITH STUDY FACTORS

					95% CI for Mean				
		Mean	SD	Std. Error	Lower B	Upper B	Minimum	Maximum	Sig
BMI	BASELINE	28.75	5.06	0.25	28.25	29.24	11.97	50.10	>0.05
	FOLLOWUP	28.45	5.13	0.26	27.95	28.96	11.97	50.06	
SGOT[0-40]	BASELINE	54.48	67.27	3.33	47.93	61.02	12.50	800.00	<0.05
	FOLLOWUP	41.15	46.72	2.42	36.40	45.90	0.81	820.70	
SGPT[0-38]	BASELINE	54.49	65.49	3.24	48.12	60.87	9.00	793.60	<0.001
	FOLLOWUP	37.38	26.37	1.37	34.70	40.07	9.00	276.60	
CAP	BASELINE	268.63	42.87	2.32	264.07	273.19	18.10	366.00	<0.001
	FOLLOWUP	253.43	47.19	3.49	246.55	260.31	3.90	400.00	
Kpa	BASELINE	13.70	21.03	1.14	11.46	15.93	2.60	264.00	>0.05
	FOLLOWUP	13.89	26.58	1.96	10.01	17.77	2.40	302.00	

ABSTRACT N°43 3/3

MEAN OF ASSOCIATIVE VARIABLES WITH STUDY FACTORS									
					95% CI for Mean				
		Mean	SD	Std. Error	Lower B	Upper B	Minimum	Maximum	Sig
BMI	BASELINE	28.75	5.06	0.25	28.25	29.24	11.97	50.10	>0.05
	FOLLOWUP	28.45	5.13	0.26	27.95	28.96	11.97	50.06	
SGOT[0-40]	BASELINE	54.48	67.27	3.33	47.93	61.02	12.50	800.00	<0.05
	FOLLOWUP	41.15	46.72	2.42	36.40	45.90	0.81	820.70	
SGPT[0-38]	BASELINE	54.49	65.49	3.24	48.12	60.87	9.00	793.60	<0.001
	FOLLOWUP	37.38	26.37	1.37	34.70	40.07	9.00	276.60	
CAP	BASELINE	268.63	42.87	2.32	264.07	273.19	18.10	366.00	<0.001
	FOLLOWUP	253.43	47.19	3.49	246.55	260.31	3.90	400.00	
Kpa	BASELINE	13.70	21.03	1.14	11.46	15.93	2.60	264.00	>0.05
	FOLLOWUP	13.89	26.58	1.96	10.01	17.77	2.40	302.00	

ABSTRACT N°44

TITLE: MATCHING-ADJUSTED INDIRECT COMPARISON (MAIC) OF RESMETIROM AND SEMAGLUTIDE FOR PATIENTS WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOHEPATITIS (MASH)

AUTHORS

Yestle Kim, Madrigal Pharmaceuticals
John O'Donnell, Madrigal Pharmaceuticals
Michael Charlton, Madrigal Pharmaceuticals
Dominic Labriola, Madrigal Pharmaceuticals
Jorn Schattenberg, Saarland University Medical Center
Rajib Dey, Cytel, Inc.
Vikas Jangra, Cytel, Inc.
Loraine Monfort, Cytel, Inc.
James Signorovitch, Analysis Group
Hoora Moradian, Cytel, Inc.

KEYWORDS

RESMETIROM, SEMAGLUTIDE, INDIRECT TREATMENT COMPARISON

OBJECTIVES

MASH is a progressive liver disease associated with high morbidity and mortality that affects approximately 5% of the global population. In the absence of head-to-head comparative trials, a matching-adjusted indirect comparison (MAIC) was conducted to evaluate the relative efficacy of oral resmetirom (80 mg and 100 mg QD) versus subcutaneous semaglutide (2.4 mg QW). The objectives were to analyze two primary endpoints: (1) resolution of steatohepatitis with ≥2-point reduction in non-alcoholic steatohepatitis activity score (NAS) and no worsening of fibrosis, and (2) fibrosis improvement by ≥1 stage without worsening of NAS.

METHODS

Patient-level data from MAESTRO-NASH (resmetirom) were weighted for comparison with aggregate data from ESSENCE (semaglutide), using mutually reported baseline characteristics identified as treatment effect modifiers or prognostic variables (age, BMI, type 2 diabetes, fibrosis stage, liver stiffness by VCTE). The primary endpoints were consistent despite differences in assessment time points between trials (i.e., Week 52 vs. Week 72). Risk ratios (RRs), which account for differences in placebo response across trials, were estimated using weighted log-binomial regression with a log link.

RESULTS

The main results showed numeric advantages with resmetirom that did not reach statistical significance. For resolution of steatohepatitis with ≥2-point reduction in NAS and no worsening of fibrosis, the RR for resmetirom versus semaglutide was 1.14 for 80 mg (effective sample size [ESS]=503.89, p=0.564, 95% confidence interval [CI]: 0.73, 1.76), and 1.24 for 100 mg (ESS=520.23, p=0.332, 95% CI: 0.81, 1.89). For fibrosis improvement by ≥1 stage with no worsening of NAS, the RR for resmetirom versus semaglutide was 1.01 for 80 mg (ESS=503.89, p=0.969, 95% CI: 0.63, 1.61) and 1.18 for 100 mg (ESS=520.23, p=0.473, 95% CI: 0.75, 1.86). Sensitivity analyses, conducted to address limitations and additional cross-trial differences, showed numerical differences favoring resmetirom without statistical significance.

CONCLUSIONS

These MAIC analyses based on all available RCT evidence showed that resmetirom achieves similar placebo-adjusted response rates at week 52 as semaglutide at week 72. The findings provide additional support for the clinical benefit of resmetirom and reinforce its role as a standard of care for MASH while underscoring the need to move beyond naïve cross-trial comparisons.

ABSTRACT N°45 1/2

TITLE: MASH AND Met-ALD HCCs SPATIAL TRANSCRIPTOMICS ANALYSIS: FIBROSIS PROGRESSION AND ALCOHOL CONSUMPTION SHAPE LIVER MICROENVIRONMENT

AUTHORS

Dr Yasmina CHOUIK, Lyon Hepatology Institute 1 Hospices Civils de Lyon, Lyon, France
Massimiliano COCCA, Lyon Hepatology Institute, Lyon, France
Marie Laure PLISSONNIER, Lyon Hepatology Institute, Hospices Civils de Lyon, 4 University Claude Bernard Lyon 1 (UCBL1), Lyon, France
Prof Kayvan MOHKAM, Lyon Hepatology Institute, Hospices Civils de Lyon, 4 University Claude Bernard Lyon 1 (UCBL1), Lyon, France
Prof Jean Yves MABRUT, Lyon Hepatology Institute, Hospices Civils de Lyon, 4 University Claude Bernard Lyon 1 (UCBL1), Lyon, France
Prof Philippe MERLE, Lyon Hepatology Institute, Hospices Civils de Lyon, 4 University Claude Bernard Lyon 1 (UCBL1), Lyon, France
Mirjam ZEISEL, Lyon Hepatology Institute, Lyon, France
Prof Cyrielle CAUSSY, Lyon Hepatology Institute, Hospices Civils de Lyon, 4 University Claude Bernard Lyon 1 (UCBL1), Lyon, France
Valerie HEVIEU, Lyon Hepatology Institute, Hospices Civils de Lyon, 4 University Claude Bernard Lyon 1 (UCBL1), Lyon, France
Prof Massimo LEVRERO, Lyon Hepatology Institute, Hospices Civils de Lyon, 4 University Claude Bernard Lyon 1 (UCBL1), Lyon, France

KEYWORDS

MASH, MetALD, HCC, SPATIAL TRANSCRIPTOMICS

OBJECTIVES

MASH accounts for 20% of HCCs in the Western world. The higher propensity for HCC development without cirrhosis in MASH underscores the unique metabolic and inflammatory micro-environment that cooperate with cancer drivers associated with metabolic syndrome and, when present, alcohol consumption. Here we investigate the metabolic and inflammatory microenvironment in tumour (T) and non tumour (NT) regions of interest (ROIs) from surgical resection samples of cirrhotic and non cirrhotic patients with HCC related to MASH and MetALD using the Digital Spatial Profiling (DSP) technology.

METHODS

Five cirrhotic (K) and 4 non cirrhotic (F1/F2/F2/F3) patients were studied. Six had no alcohol consumption (F1/F2/K/K/K/K) and 3 were MASLD-predominant Met-ALD (F2/F3/K). Spatial resolution of RNA expression was assessed using the GeoMx® Cancer Transcriptome Atlas (>1,800 genes) in FFPE tissue samples. Homogeneous areas of interest (AOI) containing PanCK or CD45 labelled cells were defined in each ROI. All cells in each AOI in the T or NT liver were analyzed separately as a mini-bulk RNA-Seq. To highlight meaningful subclusters, a pseudo-single cell approach was applied using the Seurat R packag.

RESULTS

95 ROIs (9-17 ROIs per sample) have been analyzed. After QC 71 ROIs were retained for a total of 38938 PanCK+ve cells (hepatocytes, cholangiocytes, tumor cells) and of 3410 CD45_ve cells. PCA of all ROIs showed a clear separation between PanCK AOIs and CD45 AOIs in T vs NT. Single cell specific cluster algorithms highlighted the influence of fibrosis progression in tumor samples clusterization. Focusing on CD45 ROIs, we found that the inflammatory infiltrate, richer in NT liver, displays distinct transcriptional profiles in T vs NT, with 36 down-regulated and 10 up-regulated differentially expressed genes. CD45 AOIs down-regulate lymphocyte effector pathways in T tissues. WGCNA (weighted gene co-expression network analysis) of all CD45 ROIs identified 1 module of highly connected and co-expressed genes (hub genes) associated with the tumor status. Additional modules were specific for CD45 AOIs stratified according to the presence of MASH or Met-ALD.

ABSTRACT N°45 2/2

CONCLUSIONS

Our DSP analysis unveils the contribution of fibrosis stage and alcohol consumption in shaping the tumoral and non-tumoral liver microenvironment in MASH and Met-ALD HCCs.

ABSTRACT N°46

TITLE: VALIDATION AND IMPLEMENTATION OF THE NIS2+® TEST FOR IDENTIFICATION OF PATIENTS WITH AT-RISK MASH

AUTHORS

SANDA LJUBICIC, LABCORP, GENEVA, SWITZERLAND
DEEPAK THIRUNAVUKARASU, LABCORP, INDIANAPOLIS, UNITED STATES
ZOUHER MAJD, GENFIT, S.A., LOOS, FRANCE
YACINE HAJJI, GENFIT, S.A., LOOS, FRANCE
TYSON LAGER, LABCORP, INDIANAPOLIS, UNITED STATES
ERICA TROKSA, LABCORP, INDIANAPOLIS, UNITED STATES
SARAH GRIFFIN WAGNER, LABCORP, INDIANAPOLIS, UNITED STATES
JEREMY MAGNANENSI, GENFIT, S.A., LOOS, FRANCE
HELMUT TAPIA-AGUILAR, LABCORP, INDIANAPOLIS, UNITED STATES
KOJO OSAFOL, LABCORP, INDIANAPOLIS, UNITED STATES
RICHARD RANSOM, LABCORP, INDIANAPOLIS, UNITED STATES
MATTHEW EVANS, LABCORP, INDIANAPOLIS, UNITED STATES
SATYANARLA, LABCORP, INDIANAPOLIS, UNITED STATES

KEYWORDS

MASH, LIVER FIBROSIS, NIS2+®, VALIDATION

OBJECTIVES

Newly developed non-invasive tests enable the identification of Metabolic dysfunction-Associated Steatohepatitis (MASH) patients, including those with significant or advanced liver fibrosis (F>/=2). NIS4®, a multivariate blood-based assay developed by GENFIT, has recently been optimised to allow the generation of the NIS2+® algorithm. NIS2+® is a serum-based test combining two biomarkers (YKL-40 - or CHI3L1 - and miR-34a-5p) for patients presenting with metabolic risk factors and suspicion of liver disease. Retrospective studies showed that NIS2+® offers improved robustness as compared to NIS4® for the detection at-risk MASH patients. Recently, a prospective study confirmed NIS2+® as the best test for at-risk MASH patients' detection. Using NIS2+® also improved patient selection during screening in trials by reducing liver biopsy failure rates. We performed a full validation and implementation of NIS2+® in Labcorp Central Laboratory Services (CLS).

METHODS

YKL-40 assay used established RUO Quantikine® ELISA Human Chitinase 3-like 1 immunoassay. The component miR-34a-5p required validation due to the addition of new controls and an internal spike-in calibrator. GENFIT's miR-34-5p assay involved extraction of cell-free small RNAs from human serum, followed by determination of relative levels of miR-34-5p by RT-PCR. Each of the two assays were assessed and verified for compatibility with Labcorp's globally implemented instrumentation and pre-analytical procedures. Additional validation was performed using clinical samples tested for precision and accuracy.

RESULTS

The validation of miR-34a-p assay was deemed suitable for the intended purpose as an assay to determine the relative miRNA levels in patients' serum to calculate NIS2+® score. The miR-34a-p assay passed validation criteria for precision and accuracy. NIS2+® acores obtained by Labcorp and GENFIT showed greater than 95% Pearson Correlation. In addition, there was a greater thank 90% agreement of risk stratification category match for NIS2+® scores. For high-risk category stratification, there was greater than a 90% sensitivity and Positive Predictive Value.

CONCLUSIONS

NIS2+®, a serum-based test comprising YKL-40 (CH3L1) and miR-34-5p levels, as well as gender, has been successfully implemented within our Labcorp CLS. The component miR-34-5p was validated and implemented within our CAP/CLIA-compliant laboratory. Correlation study findings support the use of NIS2+® analysis for clinical trial-associated testing.

ABSTRACT N°47 1/2

TITLE: ORGAN CROSSTALK AND TISSUE SPECIFIC INFLAMMATION IN MASLD AND MASLD-RELATED COMORBIDITIES

AUTHORS

Tabea Bieler, Division of Chronic Inflammation and Cancer, German Cancer Research Center (DKFZ), Heidelberg, Germany. Johannes Gutenberg Universität Mainz, Mainz, Germany

Dr. med Katharina Kommoss, Division of Chronic Inflammation and Cancer, German Cancer Research Center (DKFZ), Heidelberg, Germany. Department of Dermatology, University Hospital Heidelberg, Heidelberg, Germany.

Dr. Suchira Gallage, Division of Chronic Inflammation and Cancer, German Cancer Research Center (DKFZ), Heidelberg, Germany. The M3 Research Center, Institute for Interdisciplinary Research On Cancer Metabolism and Chronic Inflammation, Medical Faculty, Eberhard Karls University Tübingen, Tübingen, Germany.

Maria Kissmer, Institut für Medizinische Biometrie und Statistik (IMBI), Universitätsklinikum Freiburg, Freiburg, Germany

Dr. Shing Kam, Division of Chronic Inflammation and Cancer, German Cancer Research Center (DKFZ), Heidelberg, Germany.

Dr. Pierluigi Ramadori, Division of Chronic Inflammation and Cancer, German Cancer Research Center (DKFZ), Heidelberg, Germany.

Feng Han, Division of Chronic Inflammation and Cancer, German Cancer Research Center (DKFZ), Heidelberg, Germany.

Dr. Svenja Schühle, Division of Chronic Inflammation and Cancer, German Cancer Research Center (DKFZ), Heidelberg, Germany.

Dr. Tania Araujo Ramos, Division of Chronic Inflammation and Cancer, German Cancer Research Center (DKFZ), Heidelberg, Germany.

Aikaterini Kadianaki, Division of Chronic Inflammation and Cancer, German Cancer Research Center (DKFZ), Heidelberg, Germany.

Peng Sheng, Division of Chronic Inflammation and Cancer, German Cancer Research Center (DKFZ), Heidelberg, Germany.

Dr. med Susanne Karbach, Center for Thrombosis and Hemostasis, University Medical Center Mainz, Mainz, Germany. Center for Cardiology Cardiology I, University Medical Center Mainz, Mainz, Germany. German Center for Cardiovascular Research (DZHK) Partner Site RheinMain (Mainz), Mainz, Germany.

Dr. Ari Waisman, Institute of Molecular Medicine, University Medical Center Mainz, Mainz, Germany.

Dr. Mathias Heikenwälder, Division of Chronic Inflammation and Cancer, German Cancer Research Center (DKFZ), Heidelberg, Germany. The M3 Research Center, Institute for Interdisciplinary Research On Cancer Metabolism and Chronic Inflammation, Medical Faculty, Eberhard Karls University Tübingen, Tübingen, Germany.

KEYWORDS

MASLD, MASH, Psoriasis, γδ-T-cells, IL-17A

OBJECTIVES

Metabolic dysfunction-associated steatotic liver disease (MASLD) and its advanced form, metabolic dysfunction-associated steatohepatitis (MASH) have become the most frequent liver diseases worldwide with a global prevalence of 38%. MASLD is characterized by hepatic accumulation of triglycerides and glucose. It can progress to MASH, to fibrosis, cirrhosis, and eventually liver cancer. MASLD/MASH often coexist with other chronic inflammatory diseases like psoriasis. MASLD-psoriasis patients display higher concentrations of serum liver damage markers, as well as higher non-invasive fibrosis scores compared to MASLD patients without psoriasis. To date, it remains unclear whether the clinically observed concurrence of the two diseases is a mere coincidence, or whether there is an underlying mechanistic underpinning between both pathologies. Potential pathophysiologic connectors are similar inflammatory mechanisms involving the same immune cells and cytokines.

ABSTRACT N°47 2/2

METHODS

To investigate skin-liver crosstalk, we induced MASLD with high-fat diet (HFD) and MASH with western diet (WD) and consecutively applied Imiquimod (IMQ) to the skin to mirror psoriasis-like dermatitis.

RESULTS

High caloric diets exacerbate psoriasis-like skin inflammation by enhanced skin infiltration of inflammatory cells and triggering IL-17A production. Reciprocally, psoriasis-like dermatitis also aggravates liver steatosis and inflammation quantified by the Nonalcoholic Fatty Liver Disease Activity Score (NAS), shifting the phenotype from MASLD to MASH under HFD-conditions. Additionally, we detected an increase in IL-17A producing γδ T cells in the liver, triggered by skin inflammation, and impaired VLDL secretion from hepatocytes under psoriatic MASLD/MASH conditions.

CONCLUSIONS

Since IL-17A has been shown to be a driver cytokine in MASLD progression and impaired VLDL secretion leads to steatosis accumulation, these could represent mechanistic underpinnings of the clinically observed comorbidity of psoriasis and MASLD/MASH. Understanding the intricate relationships between these conditions is crucial for developing effective therapeutic and preventive approaches and improving overall patient outcomes.

ABSTRACT N°48

TITLE: THE IMPACT OF LIFESTYLE INTERVENTIONS AND PHARMACOLOGICAL THERAPIES ON CLINICAL OUTCOME OF MASLD/ MASH

AUTHORS

Santosh Anand, Shri venkateshwara university, Gajraula, India
Dheeraj Dubey, Shri venkateshwara university, Gajraula, India

KEYWORDS

MASLD, LIVER STIFFNESS, SAROGLITAZAR, VIT E, LIFESTYLE INTERVENTION

OBJECTIVES

Metabolic dysfunction-associated steatotic liver disease (MASLD), has emerged as a silent global epidemic, affecting approximately 25–30% of the adult population worldwide. Despite its high prevalence, the management of MASLD/MASH remains challenging. A major area of ongoing debate within the global hepatology community concerns the appropriate patient population for pharmacologic intervention, particularly in the absence of advanced fibrosis or histologic confirmation. In this study, we aimed to evaluate the therapeutic impact of specific pharmacological treatments in comparison to lifestyle interventions alone, by retrospectively analyzing clinical outcomes across MASLD cohorts with and without pharmacological therapy.

METHODS

A retrospective analysis was conducted on de-identified data from 638 patients diagnosed with MASLD/MASH, collected from various gastroenterology outpatient departments across Kolkata. The treatment duration evaluated was six months. Patients were stratified into three cohorts: Cohort 1 (n = 166) received lifestyle interventions alone without any pharmacological therapy; Cohort 2 (n = 97) received lifestyle interventions along with Vitamin E; and Cohort 3 (n = 375) received lifestyle interventions in combination with Saroglitazar. Lifestyle advice was uniformly administered across all cohorts. Paired sample t-tests were employed to assess the statistical significance of clinical outcomes within each group over the study period.

RESULTS

Over the 24-week follow-up period, liver stiffness measurement (LSM) showed a reduction of 0.29 kPa (3.4%) in Cohort 1, decreasing from 8.6± 8.5 to 8.3 ±7.9 ($p = 0.74$); a reduction of 0.59 kPa (7.71%) in Cohort 2, from 7.6 ± 4.2 to 7.1 ± 6.01 ($p = 0.42$); and a significant reduction of 2.1 kPa (15.1%) in Cohort 3, from 13.7 ± 10.8 to 11.6 ± 9.2 ($p = 0.005$). Controlled Attenuation Parameter (CAP), declined by 10.02 dB/m (3.8%) in Cohort 1 (from 264.6 ± 53.1 to 254.6 ± 41.8; $p = 0.06$), by 17.2 dB/m (5.8%) in Cohort 2 (from 298.8 ± 44.0 to 281.6 ± 38.4; $p = 0.0041$), and by 27.8 dB/m (9.2%) in Cohort 3 (from 301.6 ± 46.2 to 273.7 ± 42.8; $p < 0.001$). Significant reductions in liver enzymes (AST and ALT) were observed only in the treatment cohorts.

CONCLUSIONS

The findings suggest that targeted pharmacotherapy, particularly Saroglitazar, significantly enhances improvements in liver stiffness, steatosis, and liver enzyme levels beyond lifestyle intervention alone, supporting the evolving paradigm for early therapeutic intervention in selected MASLD/MASH patients and warranting further validation through prospective randomized trials.

Acknowledgement to our Poster Sponsors

Boehringer Ingelheim

MSD

With the partnership of

AFEF Société Française d'Hépatologie

THE FORUM For Collaborative Research™

Société francophone du diabète

TMIOA

Organized by

Arun Sanyal
Virginia Commonwealth University School of Medicine, Richmond, Virginia, USA

Lawrence Serfaty
Nouvel Hôpital Civil Strasbourg, France

Scientific committee

Jérôme Boursier
Jean-François Dufour
Scott Friedman
Fabio Marra
Massimo Pinzani
Vlad Ratziu
Jörn Schattenberg
Mohammad S. Siddiqui

PARIS MASH MEETING