

# **7<sup>TH</sup> GLOBAL MASLD** CONGRESS

LONDON HEATHROW MARRIOTT

24-25 June 2024





**#MASLDCongress** 

www.global-engage.com



# Global Engage is pleased to announce the 7<sup>th</sup> Global MASLD Congress, which is confirmed to be held on 24-25 June 2024 at the London Heathrow Marriott.

The incidence rates of MASLD (metabolic dysfunction-associated steatotic liver disease) and MASH (metabolic associated steatohepatitis) are continuing to rise year by year. As there are not any approved pharmaceutical medications on the market, the invasive liver biopsy remains the main diagnostic method and the pathogenesis is highly complex and not fully understood, there is much ongoing research currently within academia and industry to understand this disease further. There have been promising clinical developments in phase II and III clinical trials as well as a range of novel non-invasive biomarkers and diagnostic tests. This year's congress will include case studies of these, alongside new research in the disease mechanisms of MASLD and updates in the pre-clinical field.

There will be over 30 speakers at the event presenting their latest research in diagnosis, pathogenesis, and treatment of MASLD. Featuring panel and roundtable discussions and ample networking opportunities, the event provides an excellent opportunity to meet and collaborate with senior representatives from industry, hospitals, and universities, along with a dynamic exhibition room filled with providers showcasing their technologies. If you are looking to learn more from the top scientists in the field, to showcase exciting developments in your research, or to seek partnerships and funding within the industry, then this meeting is not to be missed.



	Track 1	Track 2
Day 1	Novel Biomarkers and Diagnostics	Clinical Development and Clinical Trial Data
Day 2	Recent updates in MASH pathogenesis	Clinical Development and Clinical Trial Data

- · Launched in 2018 and now in its 7th successful year
- Explores the latest scientific research, regulatory, and clinical developments in the field with a unique academic and industry joint focus
- Senior-level event with dedicated early career investigator presentation/poster award sessions to encourage development
- Attracts 40+ speakers and 150+ attendees over 2 days

# CONFERENCE SYNOPSIS

# Novel biomarkers and diagnostics:

- Liver Biopsies
- Review of current and potential biomarkers
- Non-invasive tests (NITs) for the diagnosis and prognosis of MASLD
- Improving diagnostic accuracy for identification and clinical outcome
- Patient identification
- Imaging and other non-invasive technologies

# **Recent updates in MASH pathogenesis:**

- Genetic susceptibility
- Epidemiology of MASH/MASLD
- Mitochondrial dysfunction
- Gut microbiome and MASLD
- New nomenclature- NASH to MASH and NAFLD to MASLD
- Comorbidities- diabetes, obesity
- Organ, tissue, and intercellular crosstalk
- Mechanisms of inflammation
- Epigenetics and epitranscriptomics
- Role of cholesterol in MASLD
- Fibrosis
- Hepatocellular carcinoma (HCC) and MASLD
- Role of the liver and MASLD in insulin resistance
- Liver transplants and MASLD

# Clinical Development, clinical trial data and preclinical updates:

- Current MASH Drug Development case studies
- Improving patient recruitment for clinical trials
- Endpoints in phase II/III clinical trials
- Clinical trial design
- Challenges faced in MASH/MASLD clinical trials
- Anti-obesity medications
- New therapeutic targets for MASH, MASLD and fibrosis
- Emerging combination therapies
- Gene therapies
- High throughput in vitro human and animal based MASLD models

# **Regulatory updates:**

- Global regulatory pathways
- Clinical endpoints
- Clinical safety data
- Precision medicine approaches
- Current and new regulatory guidance



# MICHAEL CHARLTON

Professor of Medicine, Chief of Hepatology and Medical Director, Transplantation Institute, University of Chicago Medicine



# LOPA MISHRA

Merinoff Endowed Chair and Professor of Medicine Co-Director, The Institute for Bioelectronic Medicine Feinstein Institutes for Medical Research & Cold Spring Harbor Laboratory Northwell Health, New York.



# REBECCA TAUB

Chief Medical Officer, President of Research & Development, Madrigal Pharmaceuticals



#### WILLIAM ALAZAWI Professor of Hepatology, Director of Research, Blizard Institute, Queen

Research, Blizard Institute, Queen Mary University of London



# ALASTAIR BURT

Professor of Precision & Molecular Pathology, Co-Lead Newcastle NIHR Biomedical Research Centre (Informatics and Precision Care), Newcastle University



#### ALEXANDRA GATZIOS Doctoral student, In Vitro Liver Disease Modelling Team, Department of In Vitro Toxicology and Dermato-Cosmetology (IVTD), Vrije Universiteit Brussel

ANNELIE FALKEVALL Senior Scientist, Karolinska Institutet



FERENC MOZES Postdoctoral Research Assistant, University of Oxford



### JUDE OBEN Consultant Gastroenterologist &

Hepatologist, Associate Professor in Experimental Hepatology, Guy's and St Thomas' Hospital, King's College London



#### Professor of Experimental Liver and Digestive Sciences, Interim Head of Department, Institute for Liver and Digestive Health, University College London, UK

KRISTA ROMBOUTS

MAITE G FERNANDEZ DE BARRENA Ramon y Cajal Researcher, Hepatology Laboratory, Centre for Applied Medical



# Research (CIMA)

MAUREEN GUICHELAAR Consultant in Gastroenterology and Hepatology, Medisch Spectrum Twente



# MICHAEL PAVLIDES

Consultant Hepatologist, Head of Liver Imaging, Principal Investigator, Oxford University Hospitals NHS Foundation Trust, Oxford Centre for Clinical Magnetic Resonance Research (OCMR), Radcliffe Department of Medicine, University of Oxford, UK

# MICHELE VACCA

NIKOLAI NAOUMOV

Associate Professor, Faculty of

Pharmacy, Universidade de Lisboa,

Professor in Clinical Biochemistry,

Postdoctoral Fellow, Karolinska

of Physicians, London

**RUI CASTRO** 

VINOOD PATEL

YING SHANG

Institutet

University of Westminster

Portugal

Associate Professor in Internal Medicine, Principal Investigator, University of Bari, Roger Williams Institute of Hepatology

Professor of Hepatology, Royal College











Executive Director, Advanz Pharma

**DIANA JULIE LEEMING** Director of Fibrosis, Hepatic and

**ALDO TRYLESINSKI** 

BAIJUN KOU Senior Principal Scientist, Regeneron Pharmaceuticals

Pulmonary Research (HPR), Nordic





JOE GOGAIN

**JOE GOGAIN** Director, Clinical R&D, SomaLogic

JUAN BASTERRA Chief Executive Officer, MikrobioMik







Bioscience

GAYE SAGINC Preclinical Programme Lead,

e-therapeutics

#### JUERGEN ECKEL Chief Executive Officer, CureDiab

Metabolic Research GmbH



# JULIO BURMAN

Vice President, European Liver Patients' Association



# LARS VERSCHUREN Scientist Applied Systems Biology, TNO

MICHAEL COOREMAN Chief Medical Officer, Inventiva



#### RADHA KRISHNAN Executive Director, Clinical Pathology Lead, MSD



**RICHARD TORSTENSON** Director Global Regulatory Affairs, AstraZeneca



SAMUEL DANIELS Director, Early Clinical Research, AstraZeneca



SCOTT HARRIS Chief Medical Officer, Altimmune



SHEELA UPADHYAYA Life Sciences Industry Consultant







VANESSA HEBDITCH Director of Policy and Communications, British Liver Trust



DIMITAR TONEV (Chair) Independent Consultant



SENIOR REPRESENTATIVE Perspectum

7<sup>TH</sup> GLOBAL MASLD CONGRESS 2024



# DAY 1 MONDAY 24<sup>TH</sup> JUNE 2024

actin. Transcriptomic analysis confirmed that thioacrylamides counter-

regulate the expression of a pro-fibrotic gene signature. In a mouse model

of liver fibrosis HK3 was found to reduce the hepatic fibrosis score and the

liver collagen content. In a unique human spheroid MASH model, the anti-

steatotic, anti-inflammatory and anti-fibrotic effect of HK3 was confirmed.

Overall, HK3 represents a novel approach for MASH therapy.

superior performance compared to existing diagnostic methods. This innovative biomarker panel offers a promising tool for effectively identifying MASLD patients highlighting the potential of translational research in enhancing diagnostic precision in liver diseases.

> 15-Minute Solution Provider Presentation For sponsorship opportunities contact Gavin Hambrook gavin@globalengage.co.uk

13:15-14:15

SAMUEL DANIELS

Lunch

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Director, Early Clinical Research, AstraZeneca Non-invasive biomarkers of liver fibrosis in drug development: Landscape review and developments Liver fibrosis is the most prognostic features of MASLD and

MASH, currently regulators require liver biopsy to determine severity of and changes in fibrosis within late stage clinical trials. Inherent limitations with liver biopsy and histological analysis bring

14:40 unique challenges to early phase drug development. Emerging data is showing the value of non-invasive tools across various context of uses. This presentation will review methodologies for determining liver fibrosis, their maturity and how they're being applied in drug development.

## **POSTER PRESENTATION FLASH PRESENTATIONS - SESSION 1:** Poster presenters and Start-ups will be provided with the

opportunity to give a flash 3-minute overview of their work

15:30-16:20



12:45-13:15

14:15-14:40

14:40

15:30

### MICHELE VACCA

Associate Professor in Internal Medicine, Principal Investigator, University of Bari, Roger Williams Institute of Hepatolog How to choose a murine model that recapitulates all the features of human MASLD?

Metabolic dysfunction-Associated Steatotic Liver Disease (MASLD) preclinical studies still need to be performed in rodents; however, the models that best recapitulate human disease are yet to be defined. The LITMUS Consortium conducted a wide-ranging retrospective review of murine models to define their metabolic relevance and ability to induce MASH-fibrosis with the aim to help with in vivo models selection, and to accelerate preclinical MASLD research.

# **ROUNDTABLE DISCUSSIONS SESSION 1:**

Roundtables are informal, small-group interactive discussions on key topics in the field. Discussion leaders will introduce sub-topics/questions for discussion and roundtable attendees are encouraged to participate actively in the session. There will be 4 roundtables occurring simultaneously during the session.



### Table 1: AI Digital Pathology for MASH Fibrosis Assessment

NIKOLAI NAOUMOV y, Royal College of Physicians, London Professor of Hepatolo Benefits of using AI Digital Pathology, alongside conventional

- histology, in assessing liver fibrosis progression and regression How AI Digital Pathology can be used in MASH clinical trials involving
- patients with F2/F3 fibrosis stage, as well as compensated MASH cirrhosis
- Can AI Digital Pathology provide better surrogate endpoints in MASH trials; what will be required to get this accepted by the Regulatory Authorities.



#### Table 2: Combination Therapies MICHAEL CHARLTON

Professor of Medicine, Chief of Hepatology and Medical Director, Transplantation Institute, University of Chicago Medicine, USA

# Afternoon Refreshments / Poster Presentations / One-to-One Presentations

#### PANEL DISCUSSION: Evaluation method challenges brought forward from HTAs for Market Access for new treatments for metabolic dysfunction associated steatohepatitis (MASH)

MASH is a fast-growing and highly prevalent threat to health worldwide, set to become a major cause of end-stage liver disease, liver cancer and the need for liver transplantation. It is an advanced manifestation of MASLD, which is likely to exceeded 30% prevalence in most middle-income and high-income countries. It is a complex disease resolving around insulin resistance, involving interactions of many organ systems as well as the paucity of symptoms in particular in early stages of the disease. As of today, there remains a medical need for (more) efficacious therapies. The panel will be discussing how the evidence needs from HTAs for demonstrating clinical relevance of a new treatment can meet the complexity of the disease presentation. The discussion will include the patient -, HTAs -and clinical demonstration perspective.

**30-Minute Solution Provider Presentation** For sponsorship opportunities contact Gavin Hambrook gavin@globalengage.co.uk



0:01

**Berlin** MICHAEL COOREMAN

Chief Medical Officer, Inventiva

SUSANNE MICHEL (Chair)



VANESSA HEBDITCH

Director of Policy and Communications, British Liver Trust

Head of HTA evidence Ascenian. Former policy lead at Department of Health England and Department of Health in



Life Sciences Industry Consultant

SHEELA UPADHYAYA

# DAY 1 MONDAY 24<sup>TH</sup> JUNE 2024



EARLY CAREER RESEARCHER PRESENTATION: FERENC MOZES

Postdoctoral Research Assistant, University of Oxford, UK Early Career Researcher: On the brink of a paradigm shift: stories from the world of non-invasive testing Clinical outcomes in patients with MASLD and MASH

are associated with histologically determined inflammation and fibrosis. Improvements in these parameters are accepted as surrogate endpoints for the purposes of regulatory approval of novel pharmaceutical treatments. Carrying out biopsies in every potential participant entering clinical trials is not feasible, raising the need of using non-invasive tests.

There is now evidence showing that non-invasive tests have similar prognostic performance to histologically assessed fibrosis stage when considering all-cause mortality, hepatocellular carcinoma, liver transplantation, or cirrhosis complications (i.e., ascites, variceal bleeding, hepatic encephalopathy, or progression to a MELD score  $\geq$ 15) as liver-related outcomes. Such findings could shift practice and regulatory pathways towards adopting non-invasive tests instead of using liver biopsies.

# ALASTAIR BURT

Professor of Precision & Molecular Pathology, Co-Lead Newcastle NIHR Biomedical Research Centre (Informatics

- and Precision Care), Newcastle University Liver biopsies in MASLD: the agony and the ecstasy Liver biopsy changes are still seen by drug regulatory authorities as mandatory endpoints for clinical trials in MASLD. However, biopsy interpretation, and in particular semi-quantitative scoring, is associated with well documented challenges.
- 17:40 This presentation will consider solutions to such problems including how we improve existing systems as well as the development and application of machine learning-derived algorithms to improve reliability.

### **MAUREEN GUICHELAAR**

Consultant in Gastroenterology and Hepatology, Medisch Spectrum Twente **MASLD and comorbidities** 

- Do comorbidities intervene in the course of MASLD?
- How do we screen and treat comorbidities? Does treatment of comorbidities also improve MASLD?

18:05-19:30

End of Day 1 / Networking Drinks Reception



16:50-17:15

17:15-17:40

17:40-18:05

#### JUAN BASTERRA fficer, MikrobioMik

EMOTION: randomised, double-blind, multicentre phase Ila study to assess efficacy, safety, and tolerability of MBK-01 (Full Spectrum & Purified Intestinal Microbiota) vs placebo for treatment of patients with metabolic dysfunctionassociated steatohepatitis

- Mikrobiomik in a nutshell
- MASH & FSPIM (Full Spectrum & Purified Intestinal Microbiota)
- Study design, objectives, and assessment criteria



#### **MICHAEL COOREMAN** edical Officer, Inventiva

MASLD, MASH and a pan-PPAR agonist: a good match The new nomenclature positions metabolic dysfunction associated

steatotic liver disease and -steatohepatitis unambiguously as the hepatic manifestation of Metabolic Syndrome. The disease biology of MASH ranges from upstream insulin resistance, altered lipid and glucose metabolism, systemic inflammation and tissue injury to progressive hepatic fibrosis. In aggregate, PPAR $\alpha$ , - $\beta/\delta$  and - $\gamma$  regulate pathways across the entire spectrum of MASH disease biology, making pharmacological activation of all three PPARs an attractive therapeutic approach. The balanced pan-PPAR agonist lanifibranor has been shown to improve insulin sensitivity in the liver and peripheral tissues incl skeletal muscle, a broad panel of markers of cardiometabolic health as well as histological steatohepatitis and fibrosis, supporting the therapeutic promise of a pan-PPAR agonist for patients with MASH.



# JULIO BURMAN

ice President, European Liver Patients' Association **Challenges in MASLD - Barriers to care for patients** 

- What ELPA does in the field of MASLD The whys and what from the patients' perspective
  - Changing the name
  - Multidisciplinary approach Diagnosis, a work in progress
- An ELPA call to action

17:15-

7:40

18



#### **KEYNOTE ADDRESS: REBECCA TAUB**

- Chief Medical Officer, President of Research & Development, Madrigal Pharmaceuticals
- Resmetirom for the treatment of adults with NASH and moderate to advanced liver fibrosis .
  - Resmetirom Phase 3 Pivotal Trial results
  - Identification of Patients with NASH using noninvasive tests Data in NASH cirrhotic patients
  - .

Global Engage Welcome Address

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**KEYNOTE ADDRESS:** LOPA MISHRA

Merinoff Endowed Chair and Professor of Medicine Co-Director, The Institute for Bioelectronic Medicine Feinstein Institutes for Medical Research & Cold Spring Harbor Laboratory Northwell Health, New York.

# Gut microbiome and immune/metabolic perturbations in MAFLD and MASH Obesity and pro-inflammatory alterations of the gut microbiome are risk factors for gastrointestinal (GI) cancers, which include hepatocellular cancer (HCC)- the

10:10

10:10-10:40

11:30-12:00

2:00-12:25

-13:1E

most common form of liver cancer with a five-year survival of less than 20%. Although the incidence due to viral hepatitis has plateaued since the wide use of effective anti-viral therapies, the increasing incidence of metabolic syndromes, including Metabolic- associated fatty liver disease (MAFLD), diabetes, and nonalcoholic steatohepatitis (MASH), predisposes more patients to develop HCC. Unfortunately, many individuals with these metabolic syndromes are not properly diagnosed or treated and are thus unaware of their increased risk for HCC. Among the pathways, as a regulator of hepatocyte proliferation and tissue regeneration, the TGF-B pathway is an important link in the development of HCC, with known pathway member alterations in up to 40% of HCCs by TCGA, and genetically

disrupting TGF-β signalling makes the animals susceptible to liver and GI cancers with altered microbiomes in multiple mouse models. Moreover, 500 million people have Alcohol dehydrogenase 2 (ALDH2) deficiency and are susceptible to liver injury and cancer- ALDH2 leads to impaired detoxification of reactive aldehydes (lipid metabolites) resulting in their toxic accumulation under chronic alcohol and high lipid intake. We have observed that high fat diet induces accumulation of toxic metabolites drive lipogenesis and oncogenesis. Interestingly, a key microbial metabolite, ammonia has also been shown to activate SREBP1 signaling and potentially promote oncogenesis. In HCC , we hypothesize that a high fat diet disrupts a regulatory network involving TGF-β. Subsequently, gut-immune homeostasis and gut microbiome are altered, generating metabolites such as ammonia producing a pro-tumorigenic environment. Therefore, a high fat diet leads to pathological interactions between microbes generating toxic metabolites, such as ammonia, that potentially divert TGF-β signaling, triggering HCC.						
<b>30-Minute Solution Provider Presentation</b> For sponsorship opportunities contact Gavin Hambrook gavin@globalengage.co.uk						
0:40-11:30 Morning Refreshments / Poster Presentations / One-to-One Presentations						
RECENT UPDATES IN MASH PATHOGENESIS SENIOR REPRESENTATIVE Perspectum	pectum () 11:30-12:00	<b>30-Minute Solution Provider Presentation</b> For sponsorship opportunities contact Gavin Hambrook gavin@globalengage.co.uk				
MAITE GARCÍA FERNÁNDEZ-BARREN/ Ramon y Cajal Researcher. Hepatology Laborat Applied Medical Research (CIMA), Pamplona, S Epigenetic and epitranscriptomic landscape progression A really critical unanswered question in MAFLD is why certain progress to severe symptomatic states, whereas another does This interindividual variability can be partially attributed to epig modifications and to recently described events known as epitt Methylation of DNA and chemical modification of histone tails mechanisms involved in the development and progression of Epitranscriptomics describe chemical RNA modifications, also and reversible, that control its structure and function without a sequence. They also play an important role in glucose and lipp while some epitranscriptomic regulators are involved in the pr MAFLD. Knowledge of the epigenetic and epitranscriptomics of events can help enormously for individual risk stratification an basis for further prevention and treatment strategies.	A ory. Centre for pain in MASLD patients not. genetic anscriptomics. are epigenetic WASLD. dynamic ffecting its d homeostasis, ogression of modifiers and d constitute the	DIANA JULIE LEEMING Director of Fibrosis, Hepatic and Pulmonary Research (HPR), Nordic Bioscience The use of neoepitope markers of the extracellular matrix to improve patient endotyping & evaluate therapeutical effects in MASLD where the matrix (ECM) plays a crucial role in MASLD, making pitope markers valuable for unraveling distinct endotypes ing neoepitope markers of the ECM as dynamic markers displaying nacodynamic effects can facilitate drug development markers can contribute to the monitoring of disease progression in LD				
ROUNDEALE DISCUSSIONS SESSION 2: Table 1: Mitochondrial targets for the treatment VINCOD PATEI Professor in Clinical Biochemistry, University of M The transition from fatty liver to inflammation is key step in the development of MAFLD. Identif the development of therapeutics. Mitochondria are central ta adaptation of hepatic fat accumulation, with the following p generally having increased flux (b-oxidation, tricarboxylic are ketogenesis, electron chain activity, and ATP synthesis). Ho accumulation continues, combined with the build of toxic or (lipid peroxides, free radical species, fatty acid mitochondria and reduced antioxidant enzyme activity, mitochondrial DN mitophagy ensues, resulting in dysfunctional mitochondrial the current agents used to treat NASH/ MAFLD include GL metformin, thiazolidinediones, which either directly or indire the burden on mitochondrial function and thus lead to a ree hepatic fat and inflammation, and improvement in insulin se Other promising antioxidant drugs include Mito-quinone, M (MitoVit-E), mitochondrial coenzyme Q10, or agents that tar and pyroptosis, may provide alternative or a combination the approach for the treatment of MAFLD.	vestminster, UK s an important ying the imental to o the initial athways cid cycle, wever, as lipid netabolites al uncouplers) A damage and biogenesis. .P-1 agonists, eactly reduce buction in ensitivity. itoVitamin E get ferroptosis erapy	<b>POSTER PRESENTATION FLASH</b> <b>PRESENTATIONS - SESSION 2:</b> Poster presenters and Start-ups will be provided with the opportunity to give a flash 3-minute overview of their work				
7 <sup>TH</sup> GLOBAL MASLD CONGRESS <b>2024</b>						



# Table 2: The road to approval of gut microbiota-based drugs for MASH/MASLD

JUAN BASTERRA Chief Executive Officer, MikrobioMik

epidemiological cohorts in Sweden

 Outlining the crucial steps needed to go from blank paper to GMPs in microbiota-based products.

- Our portfolio of clinical trials in liver diseases
- Discussing the struggle with the regulatory agencies leading up to the authorization of the phase II clinical trial for MASH/MASLD

# 13:15-14:15 Lunch



EARLY CAREER RESEARCHER PRESENTATION: YING SHANG Postdoctoral Fellow, Karolinska Institutet, Sweden Natural history of MASLD: updated data from the

14:15-14:40

In this presentation, we will share the latest findings on the natural history of MASLD in Sweden. Our research draws from several distinct cohorts, including a clinical group primarily composed of patients who underwent liver biopsy, a nationwide cohort of individuals with type 2 diabetes, and a cohort encompassing individuals from primary care, hospitals, and clinical chemistry laboratories. We will delve into the incidence rates of major adverse liver outcomes among individuals with varying risk profiles, and also explore the utility of non-invasive tests in predicting outcomes across different healthcare settings.



# EARLY CAREER RESEARCHER PRESENTATION: ALEXANDRA GATZIOS

Doctoral student, In Vitro Liver Disease Modelling Team, Department of In Vitro Toxicology and Dermato-Cosmetology (IVTD), Vrije Universiteit Brussel

#### Genetic predisposition for anti-MASH drug response: a populationbased in vitro study

Genetic determinants are important drivers of heterogeneity amongst patients suffering from metabolic dysfunction-associated steatohepatitis (MASH). In this context, our group has recently demonstrated that genetic predisposition not only influences the pathogenesis of MASH, but may also impact the response to certain treatments. Given this perspective of pharmacogenetics, this study investigates possible modifying effects of a polygenic risk score for hepatic fat content (PRS-HFC) on the anti-steatotic effects of anti-MASH drug candidates using a population-based in vitro approach. To accomplish this, we employed human skin-derived precursor-hepatic progenitor-like cells derived from different donors, which have previously demonstrated their usefulness for modelling MASH in vitro and for the screening of novel anti-MASH compounds.



# **KRISTA ROMBOUTS**

Professor of Experimental Liver and Digestive Sciences, Interim Head of Department, Institute for Liver and Digestive Health, University College London, UK

#### Exploring the impact of the genetic PNPLA3-I148M variant on primary human hepatic stellate cells (HSC) by using 3D extracellular matrix models

The PNPLA3 rs738409 C>G variant is a risk locus for fibrogenic progression of chronic liver diseases. We investigated the impact of PNPLA3-I148M variant on HSC biology using transcriptomic data of liver biopsies of obese individuals and HSC donors. Findings were validated using in vitro models based on healthy and cirrhotic human liver 3D ECM scaffolds and ECM gels bioengineered with HSC to study disease pathophysiology and pharmacological target discovery. Transcriptomic analysis highlighted shared PNPLA3-I148M-driven dysregulated pathways related to mitochondrial dysfunction/complex IV insufficiency, lower antioxidant response/increased ROS secretion, and ECM remodelling. TGFB1-endogenous inhibitor NR4A1 expression and NR4A1 targeting was linked to Akt signalling in WT-PNPLA3-HSCs; features exacerbated by cirrhotic ECM, highlighting the dual impact of the PNPLA3-I148M variant and the fibrotic microenvironment on chronic liver diseases.



#### JUDE OBEN

Consultant Gastroenterologist & Hepatologist, Associate Professor in Experimental Hepatology, Guy's and St Thomas' Hospital, King's College London

#### Trans-Generational Transmission of Obesity and NASH-MASLD - The flood is coming!

Many patients present, de novo, to Hepatology clinics, with liver fibrosis or cirrhosis. In the UK, no requirements to screen obese or type-2 diabetic (T2DM) patients, for liver disease exists. The population prevalence of T2DM in the UK and the USA is ~30%. Steatotic Liver disease (SLD) and its sub-classification, metabolic-dysfunction-associated-liver-disease (MASLD), is worldwide at ~25%. Many patients with T2DM have SLD. Maternal obesity in pregnancy and the perinatal period, programs offspring obesity and associated metabolic diseases. Mechanistically, there is an interaction between maternal genes, nutritional intake, foetal genes, and in-utero nutrient availability. Implicated molecular mechanisms in trans-generational transmission, are epigenetics, with microbiota and products. This interaction between maternal obesity, genes, epigenetics, and offspring over-nutrition sets the scene for a flood of T2DM and MASLD.

POSTER PRESENTATION FLASH PRESENTATIONS - SESSION 2: Poster presenters and Start-ups will be provided with the

opportunity to give a flash 3-minute overview of their work



-13:15

14:15

14:40

14:40-

15:05

5:05-

-15:30

15:30

-15:55

# RADHA KRISHNAN

Executive Director, Clinical Pathology Lead, MSD Next Generation Pathology: Integration of digital pathology and machine learning in MASH

Application of digital pathology and machine learning tools in liver biopsies in MASH clinical trials shows promise in reducing variability, improving reprodcibility and providing more granularity on a continuum, thereby demonstrating the added value of pathology to optimise patient diagnosis and treatment. The heterogeneity and complexity of the liver microenvironment benefit from novel deep learning approaches to decipher the complex pathophysiology in MASH. The integration of digital pathology and machine learning tools with spatial multiomic approaches including spatial lipidomics, transcriptomics and protemomics enables identifying novel targets and hypotheses generation for future MASH trials. This presentation will address the emerging role of digital pathology and machine learning tools in MASH, and its applications spanning the drug development continuum.

### ALDO TRYLESINSKI



Executive Director, Advanz Pharma Endpoints in MASH clinical trials from Phase 2 to Clinical Setting

MASLD consists of a spectrum starting from metabolic fatty liver disease, which can progress to MASH and then to fibrosis, cirrhosis, HCC or liver failure. MASLD is the major etiology for chronic liver diseases worldwide, is encountered in 30% of the world's adult population. Phase 3 pivotal studies are focused on MASH in liver fibrosis stage 2, as these patients have a higher risk of morbidity and mortality. Phase 3 primary efficacy endpoints required by regulatory agencies are based on liver histology endpoints. NITs are used in earlyphase trials and as secondary endpoints in Phase 3. In the clinical setting, liver biopsy carries significant clinical complications and important scalability and cost issues. In this review, we discuss the various endpoints in MASH clinical trials.



#### Chief Medical Officer, Altimmune Role of glucagon-containing dual and triple agonists in the treatment of obesity and MASH

Glucagon has robust effects on serum and hepatic lipids and risk reduction in cardiovascular disease and MASH. In studies of pemvidutide, our GLP-glucagon dual receptor agonist in development, we observed a 21% reduction in LDL cholesterol and > 75% relative reduction in hepatic fat content, over 50% of subjects achieving liver fat normalization. At the end of 48 weeks of treatment, the slope of the weight loss showed that weight loss was still ongoing, potentially a fundamental effect on basal metabolic rate and weight maintenance. Body composition studies also demonstrate that pemvidutide preserves lean body mass, potentially shifting energy expenditure from muscle-derived substates to beta oxidation of fatty acids. These observations add to the value of GLP-1/glucagon dual agonists in a variety of metabolic condition.



# GAYE SAGINC

SCOTT HARRIS

Preclinical Programme Lead, e-therapeutics GalOmic<sup>™</sup> siRNAs for the treatment of MASLD HepNet<sup>™</sup> is a cutting-edge computational platform

that specializes in (i) identifying novel gene targets by harnessing extensive hepatocyte-focused data sources and network biology analytics, and (ii) predicting siRNA sequences with high knockdown potency. Complementing HepNet™, the GalOmic™ chemistry platform generates siRNA therapeutics, ensuring specific and effective silencing of selected targets in hepatocytes. Our lead siRNA molecules, developed through the combined capabilities of HepNet™ and GalOmic™ platforms, are currently in pre-clinical development for multiple disease areas including Metabolic Associated Steatohepatitis, being tested for their efficacy in animal disease models, marking a significant step forward in our therapeutic pipeline.

# DAY 2 TUESDAY 25<sup>™</sup> JUNE 2024



16:20

# BAIJUN KOU

Senior Principal Scientist, Regeneron Pharmaceuticals

Combination assessment of pathological fibrosis stage and digital measurement for NASH fibrotic liver tissue to guide clinical treatment efficacy. Traditionally, fibrotic liver tissue was scored using CRN (Clinical Research Network) fibrosis stage to determine the severity and inform drug treatment efficacy. However, the recovery of fibrotic liver is a long process CRN scoring method is lacy of sensitivity to detect subtle changes. This brings a challenge to measure weather or not a drug treatment will improve liver function and life quality. We introduced a method of continuous measurement using digital quantification tool to measure % and intensity of fibrosis level in each interested area. In this method, we used Masson-Trichrome Blue and Pico-Sirius Red staining method to stain fibrotic liver tissue. Manual score to measure % and intensity of fibrosis level was performed using Masson-Trichrome blue stained section. Digitally quantification of % and intensity of fibrosis level was performed using Pico-Sirius Red stained section after scanned digitally and quantified using Halo Area Quantification Algorithm. In summary, fibrosis stage assessment is essential to measure the severity of liver damage. CRN method is foundation, Ishak method further details of portal area damage. Manual and digital measurement of fibrosis level (% and intensity) refined the progress of fibrosis and informed treatment efficacy in an early time point.

16:20

Conference Close

# **VENUE INFORMATION**

# **London Heathrow Marriott Hotel**

Bath Road, Heathrow Airport, Hayes UB3 5AN, United Kingdom www.marriott.com/hotels/travel/lhrhr-london-heathrow-marriott-hotel

Leading the way to inspiration, discover the difference at London Heathrow Marriott Hotel. Our modern guest rooms offer sumptuous bedding, soundproof windows, a Smart TV with plug-in technology and high-speed Wi-Fi access, while our upgraded suites provide extra space and access to our exclusive M Club Lounge.

Satisfy your cravings at Carluccio's, our hotel's on-site Italian restaurant, break a sweat at our well-equipped fitness centre or enjoy a rejuvenating swim in our heated indoor pool. With almost 10,000 square feet of sophisticated award-winning venue space and expert planning and catering teams, our hotel is an outstanding destination for a business meeting, wedding or social occasion.





# FREE POSTER PRESENTATIONS AND FLASH TALKS

Whether looking for funding, employment opportunities or simply wanting to share your work with a like-minded and focused group, these are an excellent way to join the heart of this congress. In order to present a poster at the forum, you need to be registered as a delegate. Please note that there is limited space available and poster space is assigned on a first-come-first-served basis (subject to checks and successful registration).

We will require the form (Downloadable Here) to be submitted.

- Poster presentations are actively encouraged at this event and as such registered academic and industry delegates are invited to present 1 poster each for free.
- Posters are displayed for the full two days of the event with breaks having a dedicated session for odd or even posters.
- NEW for 2024 We have reserved 2 x 50 minute sessions for non-vendor authors to present a flash presentation of their poster in order to showcase their work.
- We also issue a poster eBook to all attendees containing your full abstract, and you can share your poster as a PDF after the meeting if you desire (optional)



# WHAT DOES THIS MEAN FOR YOU?

# **The Marriott**

You can read the Marriott Group environmental goals here.

The London Heathrow Marriott Hotel is also a platinum GreenLeader on Tripadvisor. Click on the leaf to discover more.

# **Event App**

We have reduced waste by replacing printed documentation with an app. Make sure you have it downloaded to your devices in time for the meeting. Get Agorify on <u>Google Play</u> and <u>Apple App Store</u>.

## Catering

You will have some great food choices while you are with us but now we have worked with the caterer to increase the proportion of plant-based items. We have also built a plan with the venue to avoid waste through how they serve meals and how any leftovers are processed. Our aim is that you have some great meals, whilst with us, but with less environmental impact by the time you leave.

# Travel

An international meeting does involve travel but where it is practical, please consider more sustainable alternatives to flying. The app will also have a discussion space to arrange ride shares.

