Global Engage

7TH GLOBAL MASLD CONGRESS

LONDON HEATHROW MARRIOTT

24-25 June 2024

#MASLDCongress

www.global-engage.com

WARM WELCOME

Global Engage

Global Engage is pleased to announce the **7th 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.

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CONFERENCE SCHEDULE

	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 pre-clinical 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

CONFIRMED & RESERVED SPEAKERS

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 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

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

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

NIKOLAI NAOUMOV
Professor of Hepatology, Royal College of Physicians, London

RUI CASTRO
Associate Professor, Faculty of Pharmacy, Universidade de Lisboa, Portugal

VINOOD PATEL
Professor in Clinical Biochemistry, University of Westminster

YING SHANG
Postdoctoral Fellow, Karolinska Institutet

ALDO TRYLESINSKI
Executive Director, Advanz Pharma

BAIJUN KOU
Senior Principal Scientist, Regeneron Pharmaceuticals

DIANA JULIE LEEMING
Director of Fibrosis, Hepatic and Pulmonary Research (HPR), Nordic Bioscience

GAYE SAGINC
Preclinical Programme Lead, e-therapeutics

JUAN BASTERRA
CEO, MikrobioMik

JUERGEN ECKEL
CEO, 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

SUSANNE MICHEL
Head of HTA evidence, Ascenian. Former Policy Lead at Department of Health England and Department of Health in Berlin

VANESSA HEBDITCH
Director of Policy and Communications, British Liver Trust

SENIOR REPRESENTATIVE
SomaLogic

DIMITAR TONEV (Chair)
Independent Consultant

SENIOR REPRESENTATIVE
Perspectum

8:00-8:50 Registration / Refreshments

8:50-9:00 Global Engage Welcome Address

9:00-9:35

KEYNOTE ADDRESS:
MICHAEL CHARLTON
Professor of Medicine, Chief of Hepatology and Medical Director, Transplantation Institute, University of Chicago Medicine
Therapeutic Agent Development in MASH in 2024: On the cusp or on the brink?
The therapeutic agent development field in metabolic dysfunction associated steatohepatitis has seen a host of recent developments in clinical trials, with notable successes and challenges. We will review the key events and developments in the field and project their likely impact on the diagnosis therapy and follow up of patients with MASH. The therapeutic and diagnostic landscape, as well as epidemiological and regulatory factors driving the disease landscape will be addressed.

9:35-10:10

KEYNOTE ADDRESS:
WILLIAM ALAZAWI
Professor of Hepatology, Director of Research, Blizard Institute, Queen Mary University of London, UK
Topic TBC

10:10-10:40

SENIOR REPRESENTATIVE
SomaLogic
Topic TBC

10:40-11:30 Morning Refreshments / Poster Presentations / One-to-One Presentations

NOVEL BIOMARKERS AND DIAGNOSTICS

11:30-11:55

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
Simple non-invasive tests and liver biopsy as prognostic tool in MASLD - time to change the conversation
- Histologically assessed liver fibrosis predicts adverse outcomes in MASLD
- In a large individual participant data meta-analysis, we show that FIB4, NFS and liver stiffness measured by Fibroscan perform equally well as liver fibrosis assessment for prediction of adverse outcomes
- This has implications in multiple aspects of practice

11:55-12:20

RUI CASTRO
Associate Professor, Faculty of Pharmacy, Universidade de Lisboa, Portugal
microRNAs in MASLD: role in pathophysiology and therapeutic potential
- microRNAs (miRNAs) play a key role in MASLD pathophysiology, with its deregulation in the liver contributing for lipotoxicity, oxidative stress, metabolic inflammation and fibrogenesis.
- As such, recent studies have highlighted the use of miRNA mimics or antimiRNAs as potential therapeutic approaches for MASLD prevention and/or treatment.
- In the context of MASLD, miRNAs are also involved in inter-cellular and inter-organ communication, mainly through extracellular vesicles.
- Therefore, circulating microRNAs may be used as biomarkers for the early diagnosis and prognosis of MASLD, as well as monitoring of disease progression.

12:20-12:45

ANNELIE FALKEVALL
Senior Scientist, Karolinska Institutet, Sweden
Inhibition of VEGF-B signaling prevents non-alcoholic fatty liver disease development by targeting lipolysis in the white adipose tissue
- Pharmacological inhibition of VEGF-B (Vascular Endothelial Growth Factor B) signaling in diabetic mice reduced hepatosteatosis and NAFLD by ameliorating lipolysis in WAT.
- The beneficial effect of systemic inhibition of VEGF-B activity is due to targeting of the VEGF-B signaling pathway in the adipocytes.
- Analyses of NAFLD human subjects supported that the VEGF-B signalling pathway in the adipocytes contributes to NAFLD development.
- VEGF-B antagonism represents a novel approach to combat NAFLD by targeting hepatosteatosis through suppressing lipolysis in the WAT.

12:45-13:00

LARS VERSCHUREN
Senior Scientist, Applied Systems Biology, TNO
Development of a novel non-invasive biomarker panel for hepatic fibrosis in MASLD
This presentation focuses on addressing the growing need for non-invasive biomarkers for diagnosing and staging fibrosis in metabolic dysfunction-associated steatotic liver disease (MASLD). Starting from a diet-induced MASLD mouse model, initial biomarkers were identified through the analysis of hepatic gene expression and collagen deposition. These findings were then linked with data from liver biopsies and matched serum samples of MASLD patients, leading to the identification of a fibrosis biomarker panel. Validation in an independent patient cohort confirmed the panel's efficacy in accurately predicting various fibrosis stages, showcasing 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.

CLINICAL DEVELOPMENT, CLINICAL TRIAL DATA AND PRE-CLINICAL UPDATES

11:30-11:55

RICHARD TORSTENSON
Director, Global Regulatory Affairs, AstraZeneca
Topic: Global regulatory pathways

11:55-12:45

PANEL DISCUSSION:
Building clear regulatory guidelines for MASLD-based therapeutics
- Current regulatory guidelines for MASLD
- The impact of recent guidance on MASLD Research & Development programs
- Clinical endpoints and safety data
- Precision medicine approaches

RICHARD TORSTENSON Chair
Director, Global Regulatory Affairs, AstraZeneca

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

12:45-13:15

JUERGEN ECKEL
CEO, CureDiab Metabolic Research GmbH
Activation of the GABA-A receptor counteracts hepatic steatosis and fibrosis: A novel first-in-class approach for MASH therapy
CureDiab has identified thioacrylamide-derivatives (HK1,3,4) that mediate activation of peripheral GABA-A receptors, resulting in hepatoprotection, reduction of steatosis and an anti-fibrotic response. This was demonstrated by reduced caspase 3/7 activity in a lipotoxic model of human hepatocytes involving inhibition of STAT3 and NF-kappaB phosphorylation. In activated LX2 stellate cells, treatment with HK1,3 strongly prevented the upregulation of the profibrotic markers collagen, fibronectin and alpha-smooth muscle 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.

13:00-13:15

15-Minute Solution Provider Presentation
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12:45-13:15

Continued

13:15-14:15 Lunch

14:15-14:40

SAMUEL DANIELS
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 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.

14:15-14:40

MICHELE VACCA
Associate Professor in Internal Medicine, Principal Investigator, University of Bari, Roger Williams Institute of Hepatology
Pre-clinical MASLD models

14:40-15:30

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

14:40-15:30

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
Professor of Hepatology, Royal College of Physicians, London

- 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

Table 3: The road to approval of gut microbiota-based drugs for MASH/MASLD
JUAN BASTERRA
CEO, MikrobioMik

- 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

15:30-16:20 Afternoon Refreshments / Poster Presentations / One-to-One Presentations

16:20-16:50

30-Minute Solution Provider Presentation
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16:20-16:50

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.

SUSANNE MICHEL (Chair)
Head of HTA evidence Ascenian. Former policy lead at Department of Health England and Department of Health in Berlin

MICHAEL COOREMAN
Chief Medical Officer, Inventiva

VANESSA HEBDITCH
Director of Policy and Communications, British Liver Trust

SHEELA UPADHYAYA
Life Sciences Industry Consultant

16:50-17:15

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 ≥15) as liver-related outcomes. Such findings could shift practice and regulatory pathways towards adopting non-invasive tests instead of using liver biopsies.

17:15-17:40

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.
- 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.

17:40-18:30

PANEL DISCUSSION:
Topic: Hepatocellular carcinoma and MASLD- using AI assessment to predict HCC development

MAUREEN GUICHELAAR (Chair)
Consultant in Gastroenterology and Hepatology, Medisch Spectrum Twente

BAIJUN KOU
Senior Principal Scientist, Regeneron Pharmaceuticals

16:50-17:15

JUAN BASTERRA
CEO, MikrobioMik
EMOTION: randomised, double-blind, multicentre phase IIa study to assess efficacy, safety, and tolerability of MBK-01 (Full Spectrum & Purified Intestinal Microbiota) vs placebo for treatment of patients with metabolic dysfunction-associated steatohepatitis

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

17:15-17:40

MICHAEL COOREMAN
Chief Medical 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, PPARα, -β/δ and -γ 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.

17:40-18:05

JULIO BURMAN
Vice 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

18:05-18:30

No Track Talk

18:30-19:30 End of Day 1 / Networking Drinks Reception

8:00-8:50 Registration / Refreshments

8:50-9:00 Global Engage Welcome Address

9:00-9:35

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

9:35-10:10

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 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 non-alcoholic 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-β 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.

10:10-10:40

30-Minute Solution Provider Presentation
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10:40-11:30 Morning Refreshments / Poster Presentations / One-to-One Presentations

RECENT UPDATES IN MASH PATHOGENESIS

11:30-12:00

SENIOR REPRESENTATIVE

Perspectum

12:00-12:25

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?

12:25-13:15

ROUNDTABLE DISCUSSIONS SESSION 2:

Table 1: **Mitochondrial targets for the treatment of MAFLD**

VINOOD PATEL

Professor in Clinical Biochemistry, University of Westminster, UK

The transition from fatty liver to inflammation is an important key step in the development of MAFLD. Identifying the specific processes and altered metabolic pathways is fundamental to the development of therapeutics. Mitochondria are central to the initial adaptation of hepatic fat accumulation, with the following pathways generally having increased flux (b-oxidation, tricarboxylic acid cycle, ketogenesis, electron chain activity, and ATP synthesis). However, as lipid accumulation continues, combined with the build of toxic metabolites (lipid peroxides, free radical species, fatty acid mitochondrial uncouplers) and reduced antioxidant enzyme activity, mitochondrial DNA damage and mitophagy ensues, resulting in dysfunctional mitochondrial biogenesis. The current agents used to treat NASH/ MAFLD include GLP-1 agonists, metformin, thiazolidinediones, which either directly or indirectly reduce the burden on mitochondrial function and thus lead to a reduction in hepatic fat and inflammation, and improvement in insulin sensitivity. Other promising antioxidant drugs include Mito-quinone, MitoVitamin E (MitoVit-E), mitochondrial coenzyme Q10, or agents that target ferroptosis and pyroptosis, may provide alternative or a combination therapy approach for the treatment of MAFLD.

CLINICAL DEVELOPMENT, CLINICAL TRIAL DATA AND PRE-CLINICAL UPDATES

11:30-12:00

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

12:00-12:25

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

- The extracellular matrix (ECM) plays a crucial role in MASLD, making neoepitope markers valuable for unraveling distinct endotypes
- Utilizing neoepitope markers of the ECM as dynamic markers displaying pharmacodynamic effects can facilitate drug development
- ECM markers can contribute to the monitoring of disease progression in MASLD

12:25-13:15

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 Lunch

14:15-14:40

MAITE GARCÍA FERNÁNDEZ-BARRENA

Ramon y Cajal Researcher. Hepatology Laboratory. Centre for Applied Medical Research (CIMA), Pamplona, Spain

Epigenetic and epitranscriptomic landscape in MASLD progression

A really critical unanswered question in MAFLD is why certain patients progress to severe symptomatic states, whereas another does not. This interindividual variability can be partially attributed to epigenetic modifications and to recently described events known as epitranscriptomics. Methylation of DNA and chemical modification of histone tails are epigenetic mechanisms involved in the development and progression of MASLD. Epitranscriptomics describe chemical RNA modifications, also dynamic and reversible, that control its structure and function without affecting its sequence. They also play an important role in glucose and lipid homeostasis, while some epitranscriptomic regulators are involved in the progression of MAFLD. Knowledge of the epigenetic and epitranscriptomics modifiers and events can help enormously for individual risk stratification and constitute the basis for further prevention and treatment strategies.

14:40-15:05

EARLY CAREER RESEARCHER PRESENTATION:

YING SHANG

Postdoctoral Fellow, Karolinska Institutet, Sweden

Natural history of MASLD: updated data from the epidemiological cohorts in Sweden

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.

15:05-15:30

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 population-based 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.

15:30-15:55

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 and to Erk signalling in I148M-PNPLA3-HSCs; features exacerbated by cirrhotic ECM, highlighting the dual impact of the PNPLA3-I148M variant and the fibrotic microenvironment on chronic liver diseases.

14:15-14:40

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 digtial pathology and machine learning tools in MASH, and its applications spanning the drug development continuum.

14:40-15:05

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 early-phase 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.

15:05-15:30

SCOTT HARRIS

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.

15:30-15:55

GAYE SAGINC

Preclinical Programme Lead, e-therapeutics

GalOmic™ siRNAs for the treatment of MASLD

"HepNet™ 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 knock-down 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 (MASLD), being tested for their efficacy in animal disease models, marking a significant step forward in our therapeutic pipeline."

15:55-16:20

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.

15:55-16:20

BAIJUN KOU

Senior Principal Scientist, Regeneron Pharmaceuticals

Treatment effect on Morphological change of NASH patients Biopsy

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

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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.

POSTER PRESENTATIONS

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 Google Play and Apple App Store.

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.