3rd GLOBAL LIVER HEALTH FORUM

SCIENCE TO ADVANCE LIVER HEALTH

Friday, 7th October 2022

Virtual Forum

sanofi

Meeting overview and outcomes

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What?

The second in a series of two webinars as part of the 3rd Global Liver Health Forum. The **international webinar** was hosted via SpotMe and comprised **prerecorded presentations** and **live Q&A** sessions

Who?

Over **433 HCPs** connected live from **29 countries**. Presentations were delivered by 4 international **scientific experts**. Hosted by **Branko Popovic (Sanofi)**, chaired by **Prof. Hartleb** and moderated by **Andrea Cole (Ashfield Healthcare Communications)**

Why?

Explore the **key factors** and **comorbidities influencing MAFLD**, the **potential mechanisms** of **EPL treatment**, and **new initiatives** supporting the **liver health landscape**

Provide an environment where **experts can share their insights** and priorities in the area of liver diseases

Meeting metrics

Total participants

433

Number of participating countries

29

Top participating countries

Romania, Poland, Egypt

The webinar was led by a prestigious faculty:

Professor Hartleb is the Head of the Department of Gastroenterology and Hepatology at the Medical University of Silesia in Katowice, Poland, where he also holds a position as Head of the Scientific Committee of the School of Medicine. Professor Hartleb is also the Editor-in-Chief of the national scientific journal *Gastroenterologica Praktyczna (Practical Gastroenterology)*.

Professor Fricker is a Professor at the Institute of Pharmacy and Molecular Biotechnology in the Faculty of Biosciences, University of Heidelberg, Germany. Professor Fricker is Head of the Technology Transfer Centre Biopharmacy and Analytics in Heidelberg, as well as initiator of HEIDELTEC GmbH, a university spin-off company dealing with oral peptide drug delivery.

Professor Mao is Director of the Research Centre of Shanghai Fatty Liver Disease, and Chief Physician and Professor of the Gastroenterology Department at Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China. Professor Mao has conducted numerous clinical trials as principal investigator in the field of gastroenterology and liver disease in China.

Donna R. Cryer is Founder and CEO of the Global Liver Institute, the leading patient advocacy organisation in liver health, convening more than 200 organisations across 70 countries. A graduate of Harvard and Georgetown Law, she serves on several boards, including Sibley Memorial Hospital/Johns Hopkins Medicine and the Council of Medical Speciality Societies.

Professor Hartleb

Department of Gastroenterology and Hepatology,
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CARDIOVASCULAR AND METABOLIC RISKS OF MAFLD: IMPORTANT CONSIDERATIONS FOR CLINICAL PRACTICE

MAFLD is a multi-systemic disease that increases the risk of T2DM and CVD

MAFLD is a multi-system disorder.[1] Diet-induced obesity drives metabolic stress, insulin resistance in adipose tissue and systemic inflammation and fibrosis, increasing the risk of T2DM and metabolic syndrome.[1] MAFLD can present with a wide spectrum of other extrahepatic diseases such as chronic kidney disease, extrahepatic malignancies and cognitive disorders.[2] The most advanced stage of MAFLD, NASH, has systemic effects throughout the body and is associated with the greatest risk of cardiometabolic comorbidities.[1,2] Indeed, the prevalence of T2DM among the general population of the USA is 14%, and increases to 22.5% among those with non-NASH MAFLD and 43.6% in those with NASH.[3]

Multiple studies confirm the relationship between MAFLD and CVD

MAFLD has been shown to increase the risk of subclinical atherosclerosis, CAD and CV events. In a meta-analysis of 14 studies, including 2,932 patients, there was a higher prevalence of CIMT (35.1% vs 21.8%; p<0.0001) and CAD (80.4% vs 60.7%; p<0.0001) among patients with MAFLD versus those without, respectively.[4] In addition, a prospective study demonstrated a higher prevalence of CV events among patients with MAFLD versus those without (19% vs 10%, respectively; p=0.007), with one of the strongest predictors of CV events being hepatic steatosis (HR=1.99; 95% CI: 1.01–3.94).[5]

MAFLD/NASH have also been associated with an increased risk of mortality. In a cohort study to re-evaluate survival and cause of death in patients with MAFLD, survival of those with NASH was reduced versus the general population, with these patients more often dying from CV and liver-related causes (p=0.04 for both).[6] Similarly, another population-based cohort study revealed a higher rate of mortality in patients with MAFLD versus those without MAFLD, with the three main causes of death cited as cancers, CV events, cirrhosis and HCC.[7] These findings have been corroborated by a multicentre, retrospective study of 10,071 patients with and without MAFLD in China.[8] Those with MAFLD had higher proportions of death due to underlying CVD and liver-related diseases than the general population, and these proportions positively correlated with degree of steatosis.[8]

Furthermore, the severity of liver fibrosis correlates with CV risk. In a prospective cohort study of 288 patients with MAFLD, of whom 26 (9.1%) experienced an incident CV event, advanced fibrosis (stage 3–4) on biopsy was shown to be a significant predictor of incident CVD (HR=2.86; 95% CI: 1.36–6.04).[9]

There exists a bidirectional relationship between MAFLD and T2DM

The relationship between MAFLD and T2DM is complex.[10] Though the mechanisms underlying the relationship are complex and not completely understood, it is known that MAFLD promotes worsening insulin resistance and increases the risk of T2DM, atherogenic dyslipidaemia and CVD, while T2DM increases the risk of NASH, cirrhosis and HCC.[10]

CV risk should be assessed in patients with MAFLD

SCORE2, a prediction model to estimate 10-year fatal and non-fatal CVD risk in individuals without previous CVD or diabetes (aged 40–69 years) in Europe, incorporates typical CV risk factors, such as age, smoking, blood pressure and cholesterol levels.[11] However, there is a need to develop a tool that evaluates the impact of MAFLD and NASH on the prediction of CV events.

Therapeutic approaches for managing MAFLD and associated comorbidities

Therapeutic approaches include strategies for weight loss, treatment of T2DM and other cardiometabolic comorbidities, liver-directed treatment and reducing end-stage complications. In addition, EPL has been shown to exert many potential benefits in liver diseases, including regeneration of liver cells,[12–14] detoxification,[15–17] and cell-protective effects.[12,14,17] In the RESTORE study, which ranked the five most recommended supportive treatments by the top three criteria among GEs and GPs, the top three criteria were efficacy, tolerability and quality of life improvement, and EPL was regarded as having a good efficacy and tolerability in comparison with other interventions.[18] Moreover, a direct meta-analysis of RCTs comparing the effect of treatment with EPL + AD versus AD therapy alone, indicates that EPL + AD was associated with a significantly greater reduction in ALT (p=0.0003), triglyceride (p<0.0001) and total cholesterol (p<0.0001) levels than AD alone.[19]

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AD, antidiabetic; ALT, alanine aminotransferase; CAD, coronary artery disease; CI, confidence interval; CIMT, carotid intima-media thickness; CV, cardiovascular; CVD, cardiovascular disease; EPL, essential phospholipids; GE, gastroenterologist; GP, general practitioner; HCC, hepatocellular carcinoma; HR, hazard ratio; MAFLD, metabolic-dysfunction associated fatty liver disease; NASH, non-alcoholic steatohepatitis; RCT, randomised controlled trial; T2DM, type 2 diabetes mellitus.

Professor Fricker

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THE POTENTIAL MOLECULAR MECHANISM OF EPL: INSIGHTS FROM EASL 2022

Introduction to EPL

The most abundant phospholipids that exist in mammalian tissues include PC and PE and are essential components in maintaining healthy cell membranes.[1] EPL are a hepatoprotective treatment that comprises a highly purified extract of PPC molecules from soybeans; the main active ingredient is DLPC, which corresponds to approximately 52% of the phospholipids in EPL.[2] NAFLD/MAFLD is the most common liver disease worldwide, and EPL have been shown to exert lipid-regulating properties, as well as multiple membrane protective effects.[2–4] While the therapeutic effects for such lipids have previously been described using clinical observations, fairly little is known about the molecular mechanisms of EPL.[2]

The *in-vitro* effect of EPL on pro-inflammatory cytokines

The effects of EPL and its constituents, PPC and PI on hepatocyte function were investigated in a recent study using steatosis cell lines *in vitro*.[5] EPL (0.1 and 0.25 mg/mL), PPC and PI (both at 0.1 and 1 mg/mL) in human hepatocyte cell lines (HepG2, HepaRG, steatotic HepaRG) versus untreated cells were assessed on the release of pro-inflammatory cytokines caused by treatment with LPS (a commonly studied glycolipid produced by most gram-negative bacteria) and lipid metabolising enzymes.[5]

In HepaRG cells treated with LPS, the addition of EPL (0.25 mg/mL; $p=0.0063$), PPC (1 mg/mL; $p<0.0001$) and PI (0.1 mg/mL; $p=0.0023$) significantly reduced the release of IL-6. However, in steatosis, LPS-treated HepaRG cell lines, treatment with EPL (0.1 mg/mL; $p<0.0001$) and PI (1 mg/mL; $p=0.0029$) led to an increase in the release of IL-6.[5] The reduction of IL-6 observed in the HepaRG cell lines supports the anti-inflammatory properties of EPL and its constituents, while the reduced activity in steatotic cells suggests a protective effect against the further development of steatosis.[5]

The *in-vitro* effect of EPL on lipid metabolising enzymes

There are many essential elements involved in lipogenesis.[6,7] For example, the enzyme G6PD is involved in the pathway that produces NADPH, which is required for fatty acid biosynthesis. Increased G6PD activity has previously been linked with fatty liver in rats.[7] G6PD activity remained unchanged with EPL, PPC and PI treatment in LPS-treated HepaRG and steatotic HepaRG cells.[5] Expression of rate-limiting enzymes such as acyl coenzyme A oxidase, which are higher in patients with NAFLD, have also shown to be reduced in LPS-treated HepaRG cell lines treated with EPL, PPC and PI.[5,8]

The build-up of fat in NAFLD is caused by an excess of the triglycerides and fatty acids that accumulate in the liver.[9] Fatty acid influx and synthesis within the liver can therefore lead to accumulation of fat deposits and steatosis. FAS, the enzyme that catalyses the final stage of fatty acid synthesis in the liver, may therefore have an association with steatosis.[9]

In LPS-treated HepaRG cells, FAS expression remained unchanged with EPL, PPC and PI treatment, whereas expression decreased with the same treatments in LPS-treated steatotic HepaRG cells.[5] Similarly, in rats with induced fatty liver, those receiving dietary PC showed no increase in FAS expression, whereas those without dietary PC did.[7] This suggests that PC administration in steatotic HepaRG cells may lead to a reduction in hepatically-produced fatty acids.[5]

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DLPC, 1,2-di-linoleoyl phosphatidylcholine; EPL, essential phospholipids; FAS, fatty acid synthase; G6PD, glucose-6-phosphate dehydrogenase; IL-6, interleukin-6; LPS, lipopolysaccharide; NADPH, nicotinamide adenine dinucleotide phosphate; MAFLD, metabolic associated fatty liver disease; NAFLD, non-alcoholic fatty liver disease; PC, phosphatidylcholine; PE, phosphatidylethanolamine; PI, phosphatidylinositol; PPC, polyenylphosphatidylcholine.

Professor Mao

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DIAGNOSIS AND TREATMENT OF DRUG-INDUCED LIVER INJURY: GUIDELINES AND PRACTICE

Epidemiology, types, and causes of DILI

DILI is a rare condition within the general population; however, the prevalence of the condition is gradually increasing in hospitalised patients.[1] Among patients with unexplained liver conditions such as hepatic biochemical abnormalities, jaundice or ALF, DILI is a common aetiology.[1] In the USA, most cases of DILI in patients with new onset non-alcoholic jaundice are attributed to APAP, with a prevalence of ~4%. The proportion of DILI within the ALF population is also increasing; for example, in the USA, DILI caused by APAP and (i)DILI accounts or >50% of all cases of ALF.[1]

DILI is typically classified as direct hepatotoxicity (a frequent, predictable and dose-related condition), idiosyncratic hepatotoxicity (a rare form of liver injury that is neither predictable nor dose-related), or indirect hepatotoxicity (a non-dose-related condition that can be predicted in some cases). Indirect DILI presents a new therapeutic challenge due to its dose-agnostic nature, as the condition is thought to be caused by the indirect action of an agent on the liver or immune system. It has a delayed onset and is more common than idiosyncratic hepatotoxicity but less common than direct hepatotoxicity.[2]

Many different causes of DILI have been identified and the leading cause typically varies from country to country. In Spain and France, the leading cause of DILI is anti-infectious agents, while antibiotics, antimicrobial drugs and anti-inflammatory drugs are the leading causes in Iceland, the USA and Japan, respectively. Conversely, in Korea the leading cause of DILI is herbal medications, in Singapore it's Chinese traditional CAM, in India it's anti-TB drugs, and TCM or HDS are the leading causes of DILI in China.[1] In general, Asia-Pacific regions show a higher incidence of HDS-induced liver injury in DILI than Europe and the USA.[1]

Factors contributing to the development of DILI

A variety of risk factors that are considered to contribute to the risk of DILI have been identified; however, not all-cause risk factors have been confirmed.[3] DILI events tend to result from combined effects of the first exposure from potential hepatotoxic drugs, genetic and non-genetic risk factors, and adaptive injury repair mechanisms.[1] More recently, due to the consideration of genome-wide association studies, key HLA alleles that influence the susceptibility to DILI caused by specific drugs have been identified. Clinically, the negative predictive value of HLA alleles could be used to exclude certain drugs as a cause of DILI.[1]

ACG-DILI guidelines for the diagnosis of DILI

Internationally, there are different DILI clinical guidelines which cover multiple types of DILI. DILI is diagnosed by exclusion, through a careful assessment of other aetiologies of liver disease.[1] Other possible causes of liver injury are excluded based on: clinical history, including a thorough history of the patients intake of drugs and HDS; serum biochemical tests; liver imaging; and/or biopsy.[1,4] When obtaining history on the indication and use of drugs and HDS, it is important to have a complete list of all agents, exposure times of each agent and also gather washout data by conducting liver biochemistries.[4]

The ACG-DILI guidelines recommends differential diagnostic strategies for suspected DILI. Liver biopsies are recommended to assist diagnosis in many different circumstances, including cases of DILI where there has been continued use or re-exposure to the implicated agent.[4]

Recommendations for treatment of DILI, according to different guidelines

It is widely agreed across the many different guidelines for DILI treatment strategies, that the most important management strategy when DILI is suspected is to discontinue the offending agent.[4–9] However, guidelines often provide differing recommendations regarding other treatment strategies. Both the ACG (2021)[4] and the CIOMS (2020)[6] guidelines recommend the use of corticosteroids in DILI patients with AIH-like features, whereas CSH guidelines (2015) recommend corticosteroids for the treatment of patients with immuno-allergic or autoimmune features.[8] A retrospective analysis study investigating the use of steroids in ALF in 361 ALF cases, including 131 of the aetiology DILI, from 1998 to 2007 found that corticosteroids did not improve overall survival or spontaneous survival (survival without transplant) in drug-induced ALF.[10] In an open-label, controlled study in 150 patients with solid malignant tumours, lower incidence of liver dysfunction with adjunctive EPL treatment after chemotherapy (16.8% vs 44.2%, p<0.0001) and lower hepatoxicity grade (2.5% vs 13.9%, p<0.0001) were observed.[11]

The relationship between DILI and COVID-19

Patients with COVID-19 often show abnormalities in liver tests, though the cause of this is currently unknown. A systematic review was conducted to characterise the role of conventional drugs in causing DILI using data from 393 patients with DILI and COVID-19; the results of the review showed that the most common cause of DILI was anti-viral drugs given empirically for their known therapeutic efficacy in other viral infections.[12] In addition, for patients with MAFLD, the risk of DILI in patients with COVID-19 is increased, as they are much more likely to be hospitalised and receive antiviral agents to treat severe systemic inflammation.[13]

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ACG, American Society of Gastroenterology; AIH, autoimmune hepatitis; ALF, acute liver failure; APAP, acetaminophen; CAM, complementary and alternative medicines; CIOMS, Council for International Organizations of Medical Sciences; COVID-19, coronavirus disease 2019; CSH, Chinese Society of Hepatology; (i)DILI, (idiosyncratic) drug-induced liver injury; EPL, essential phospholipids; HDS, herbal and dietary supplements; HLA, human leucocyte antigen; MAFLD, metabolic-dysfunction associated fatty liver disease; TB, tuberculosis; TCM, traditional Chinese Medicine.

Donna R. Cryer

Global Liver Institute, Washington, DC, USA

DEFYING THE TRENDS: LEVERAGING LIVER HEALTH TO IMPROVE PATIENT OUTCOMES

The Global Liver Institute

The Global Liver Institute (GLI) is a non-profit organisation that aims to bridge the knowledge gap between patients and HCPs surrounding unmet needs in liver care. It promotes innovation and collaboration between patients impacted by liver diseases and organisations such as AASLD, with the goals of destigmatising liver conditions and improving patient outcomes.[1]

The importance of advocacy groups in the 21st century

Despite the plethora of medical advances in the 21st century, sedentary lifestyles and high-calorie, high-fat diets have led to public health emergencies that impact many individuals and may result in poorer outcomes for patients with liver diseases.[2] The increasing rates of obesity,[3] type 2 diabetes and heart disease add to the burden of cardiometabolic comorbidities on patients with MAFLD.[4,5] Health trends encourage the use of herbal and dietary supplements, which do not require the same FDA screening and approval as other drugs.[6] Use of these supplements has been proportionally associated with increased rates of DILI,[6] and the full effects of the COVID-19 pandemic on liver care have yet to be determined. As well as COVID-19 infection resulting in increased ALT and AST in patients with liver diseases,[7] the COVID-19 lockdowns have been associated with an increase in the number of ALD -related deaths and have disproportionately impacted minority communities.[1,8] For these reasons, the GLI has launched several initiatives to advocate for patients in the liver health space and to highlight the impact on minority communities.[1]

- **The NASH Council –** Launched in 2017 at the Milken Institute School of Public Health, the GLI NASH Council highlights the importance around the urgency of developing processes for quantifying and addressing the NAFLD and NASH epidemics in the USA and around the world
- **International NASH Day –** International NASH Day is a public health campaign launched in 2018 to raise awareness and urgency around NAFLD and NASH. The 5th International NASH Day held this year achieved widespread engagement from across the globe
- **Beyond the Biopsy –** Invasive diagnostic techniques can be a barrier to diagnosis and may perpetuate the cycle of late diagnosis and poor clinical outcomes. The Beyond the Biopsy awareness campaign is dedicated to accelerating the acceptance and adoption of non-invasive diagnostic techniques
- **GLI Live –** The shift to virtual engagement following the COVID-19 lockdowns resulted in the emergence of GLI Live, a weekly educational show providing a platform to share information on liver care
- **Liver Health is Public Health –** With the aim to elevate liver health awareness in the public health agenda, Liver Health is Public Health is a global initiative to educate the public on liver health and disease prevention. The programme focuses on reaching patients across the different cultures and socioeconomic backgrounds

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AASLD, American Association for the Study of Liver Diseases; ALD, alcoholic liver disease; ALT, alanine transaminase; AST, aspartate transaminase; COVID-19, coronavirus disease; DILI, drug-induced liver injury; FDA, Food and Drug Administration; GLI, Global Liver Institute; HCP, healthcare professional; MAFLD, metabolic associated fatty liver disease; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis.

Q&A SESSIONS

Prof. Hartleb

Considering the close association between MAFLD and cardiometabolic risk factors, is it advisable to monitor patients with diabetes and other cardiometabolic comorbidities for MAFLD?

Firstly, it should be noted that screening for MAFLD in the general population is not recommended, as it is not considered cost-effective. However, patients with T2D and obesity are a high-risk population for NASH and fibrosis, and screening in these populations is very important as early diagnosis and intervention can halt disease progression.

Recent guidelines by the American Association of Clinical Endocrinology noted that in patients with T2D, clinicians should consider screening for clinically significant fibrosis using the Fibrosis-4 score, even if they have normal liver enzyme levels.

Is Essentiale® recommended for the treatment of MAFLD in any management guidelines?

EPL are not yet recommended by most leading hepatology organisations such as EASL or ASLD. However, Chinese consensus reports on MAFLD published in 2010 and 2013 took into consideration EPL as adjunctive treatment to lifestyle modification. According to these reports, anti-inflammatory and hepatoprotective treatments should be considered in patients with histologically proven NASH, those showing high levels of transaminases, taking hepatotoxic drugs, or having concurrent viral hepatitis. EPL are not recommended for more severe stages of liver disease as evidence of their effectiveness is lacking in these populations. In Poland, prolonged therapy with EPL was justified only in the case of significant reduction in aminotransferases.

MAFLD is considered a multi-organ disease – how can its management be implemented into clinical practice? Would a multi-disciplinary approach be needed for optimal management?

While a multi-disciplinary strategy would be the best approach, it is not always achievable. In practice, an ultrasound should be performed in every patient with metabolic risk, and ALT activity measured for diagnosis of MAFLD. Assessment of the comorbidities associated with MAFLD, such as cardiometabolic disorders and obesity, should be considered in the early stages of management, where optimal treatment can be provided. Treatment with statins, as one example, has been shown to reduce the risk of hepatocellular carcinoma, indicating the multi-organ nature of MAFLD.

Could you elaborate on the association between chronic kidney disease and MAFLD?

The frequency of chronic kidney disease (CKD) is seen more so in patients with MAFLD than the general population. CKD is defined as decreased glomerular filtration rate below 60 mL/min, but a direct relationship between CKD and MAFLD is unknown. Both conditions, however, share similar risk factors in arterial hypertension and diabetes, which can progress from kidney and liver disease. In this pathogenic chain, the kidney and liver are both impacted.

Would you recommend a hepatoprotective treatment in a patient with MAFLD and cardiometabolic comorbidities?

There is a place for hepatoprotective treatments, such as EPL, during the earlier and reversible stages of MAFLD, where they would be provided as adjunctive treatments in addition to lifestyle modifications. However, these would not be suitable for later-stage disease such as NASH and fibrosis.

How can we work more closely with specialists in endocrinology and cardiology to adopt liver health into their clinical considerations?

The bidirectional relationship between comorbidities such as cardiometabolic risk and liver disease have increasingly been studied and adopted by guidelines since 2018. These changes were thought to naturally lead to better considerations by specialists outside of liver health.

Prof. Fricker

What might be the implications of IL-6 decrease in HepaRG cells?

The observations of IL-6 decrease in HepaRG cells within the study indicates that in-vivo there may be an acute phase response and release of IL-6. On the other hand, it is known that separate from its role in acute phase response, IL-6 may be beneficial in the long-term, as it promotes cytoprotection, regeneration and modulates metabolic activity of liver cells. This suggests that the slight increase of IL-6 observed in steatosis HepaRG cells is also beneficial in-vivo.

How could a reduction in FAS secretion be beneficial in patients with NAFLD?

The secretion of FAS is directly correlated with accumulation of lipids and fat in the liver. Therefore, reduction of FAS secretion is likely to decrease the accumulation of these components within the liver.

Why do imbalances in the hepatic cell membrane affect liver function?

One factor includes reduced transporter function in the liver cell membrane, particularly in the canicular membrane, where excretory transport proteins exist. Most of these proteins are impaired in liver diseases, and EPL has been shown to improve the function of these transport proteins in pre-clinical studies.

How is LCAT involved in the pathogenesis of MAFLD, and how can a reduction of LCAT result in improved outcomes for patients with liver diseases?

It is difficult to determine the association of LCAT reduction and MAFLD in clinical cases. Currently, only in-vitro studies exist examining modification of LCAT with treatment of cells with EPL, thus, further research is needed to understand MAFLD pathogenesis.

What could be the next steps to investigate following the results of the in-vitro study examining the effects of EPL treatment on cytokines and metabolising enzymes?

Animal models would be the next step to better understand the pathology of EPL treatments. Examining the amount of EPL that is processed by the liver and its effectiveness in alleviating liver damage can provide data to support human studies.

Prof. Mao

In addition to suspending the offending drug, what would your recommendation be for someone with recently diagnosed DILI?

In clinical practice, some patients may not mention exposure to the suspected drug to their clinician, thus, in patients with unexplained liver disease, a thorough history of drug use must be obtained.

What are the long-term implications of DILI on liver function?

The outcome of DILI can vary among patients. Most cases of DILI are improved after suspending the offending drugs, however, in a small number of cases, acute liver failure can be seen. In addition to this, a small number of cases of acute liver failure may result in chronic disease, where liver biochemistry remains abnormal for 1–2 years.

In clinical practice, a challenge is to make the distinction between DILI and acute-onset, autoimmune hepatitis. How would you address this issue?

The differentiation between drug-induced autoimmune hepatitis (DIAH) and acute-onset autoimmune hepatitis (AIH) is very challenging, as these are difficult to diagnose even after liver biopsy. An important factor to consider is the response after withdrawal of steroids. In cases of AIH, withdrawal of steroids often leads to relapse of liver injury, whereas this is rarely observed in patients with DIAH.

As guidelines do not consistently recommend treatment pathways for children with DILI, what data would be needed to incorporate management recommendations into these guidelines?

Currently, only the guidelines by the American College of Gastroenterology discuss the topic of children with DILI. More research is needed in this target population before guidelines and recommendations can be developed.

Donna R. Cryer

How can the adoption of non-invasive diagnostics be integrated into best practice and guidelines?

The first step was to highlight the inadequacies and risks of liver biopsy to accelerate innovation of non-invasive tests. Working with EASL on their changes to non-invasive diagnostic guidelines, in addition to communicating with ASLD and other medical societies has allowed the GLI to provide information to regulators during externally led patient-focussed drug development meetings and echo these discussions to the Food and Drug Administration. Clinical practice continues to rapidly adopt either imaging or serum markers, which are easier to integrate into the management workflow, rather than biopsy. In practice, very few clinicians now diagnose NASH with biopsy, thus, the clinical trial and regulatory authorities also need to adapt to these changes.

How can regions without a strong liver health awareness programme improve their collaboration with other partners?

The GLI has been willing to collaborate with many regions, as demonstrated by their materials being available in 16 different languages. HCPs can provide this information to their patients.

The GLI has worked with a variety of regions to plan dissemination of content for NASH or liver cancer, as well as provide a base where existing connections to organisations within the same region can be used to contact other partners, such as researchers or clinicians.

How has the COVID-19 pandemic impacted care for patients with liver diseases? Which populations have been most affected?

One factor for the increase in prevalence of liver disease may include the conditions associated with confinement during the pandemic. For example, cases of alcohol-related liver disease or obesity were found to increase during this period. Thus, the increasing prevalence of liver disease can be associated with many other causes and comorbidities. Another issue is that patients have been reluctant to return to healthcare, delaying diagnosis and management.

One goal of the GLI has been to educate communities on the importance of regular health checks as well as vaccinations to reduce the risk for adverse effects due to COVID-19 infection.

UPCOMING

The next Global Liver Health Forum will take place in 2023. Stay tuned!

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