EASL™
The Home of Hepatology

THE DIGITAL INTERNATIONAL LIVER CONGRESS 2020

27-29 AUGUST 2020

Press & Media Kit

CONTENTS

ABOUT EASL

EASL, The European Association for the Study of the Liver, is a medical association dedicated to pursuing excellence in liver research, clinical practice of liver disorders, and in providing education to all those interested in hepatology.

While the roots of the association were founded in Europe in 1966, EASL continues to engage globally with all stakeholders in the liver field wherever they are based. Our aim is to spread knowledge and expertise in best practices and the latest scientific breakthroughs in hepatology.

The European Association for the Study of the Liver mission is to be the Home of Hepatology so that all who are involved with treating liver disease can realise their full potential to cure and prevent it. The purpose of the association is to promote communication between European experts interested in the liver and its disorders.

ABOUT THE DIGITAL INTERNATIONAL LIVER CONGRESS (ILC)

This annual congress is EASL's flagship event, attracting scientific and medical experts from around the world to learn about the latest in liver research and exchange clinical experience. Attending specialists present, share, debate and conclude on the latest science and research in hepatology, working to enhance the treatment and management of liver disease in clinical practice.

This year, the congress is being held entirely digitally due to the global health situation. The Digital International Liver Congress™ 2020 will take place from 27–29 August 2020.

CONTACT

The Digital ILC 2020 Press Team look forward to liaising with you throughout the Congress.

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WELCOME

Dear colleagues, friends and participants,

During these unprecedented times, we are all adapting our work and research to respond to the COVID-19 public health crisis. My sincere gratitude goes to our colleagues, including nurses, doctors, other health professionals and key workers for their dedication, hard work, and flexibility.

One of the challenges that EASL has faced relates to the delivery of a safe International Liver Congress. Unfortunately, due to the ongoing global pandemic we do not feel it is appropriate to hold a face-to-face event.

Having considered the different options carefully, we believe it is important for the liver community to connect and to share the latest in data, education, and science. We have therefore decided to transition the onsite International Liver Congress™ 2020 to an innovative digital event, The Digital International Liver Congress™ 2020, which takes place from Thursday, 27 to Saturday, 29 August 2020, and will bring you cutting-edge content and extensive interactivity throughout.

Notably, EASL has been livestreaming all sessions at its events since 2019 and has been providing educational content online through the EASL Campus. This experience of delivering online content to the liver community gives us the platform to go up to the next level at The Digital International Liver Congress™ 2020.

Thank you for your continuing support and we look forward to welcoming you to The Digital International Liver Congress™ 2020.

With very best wishes

Prof. Philip Newsome

EASL Secretary General

PRESS BRIEFING

A virtual press briefing was held on Wednesday 19 August 2020 at 11:00 CEST, hosted by Professor Thomas Berg.

All members of the press are able to view the press briefing to obtain exclusive first-hand information of some of the most exciting abstracts at this year's congress from the authors themselves.

Press Briefing Schedule

Presenter	Topic
Thomas Berg	COVID-19 and the Liver
Jasmohan Bajaj	AS081 Fecal Microbial Transplant Reduces Short-Term Cravings, Improves Quality of Life and Microbial Diversity in Cirrhosis and Alcohol Use Disorder: A Randomized, Placebo-Controlled, Clinical Trial
Ben Goudsmit	GS05 Validation of the Model for End-stage Liver Disease sodium score for the Eurotransplant region.
All	Q&A

Accessing the Briefing

You can request a recording of the press briefing or a 1-2-1 interview with the presenters by emailing press@easloffice.eu.

All presentations are under embargo and we ask that this is respected. This is stated at the start of each presentation.

PRESS RELEASES

27 August 2020

This section includes all press releases embargoed until 00:01 CEST on Thursday 27 August 2020

Please kindly respect the embargo.

PRESS RELEASE

EMBARGO: 00:01 CEST, THURSDAY, 27 AUGUST, 2020

Two novel treatments show promise in improving biomarkers of NASH pathology

Digital ILC 2020: As new data highlight the increasing prevalence of NAFLD, two new treatments have demonstrated reductions in ALT, hepatic fat and other indicators of liver disease, including in patients with type 2 diabetes

EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER (EASL)

27 August 2020: Improvements in multiple biomarkers of non-alcoholic steatohepatitis (NASH) progression, reported in clinical studies across two drug classes, were presented today at The Digital International Liver Congress™ (DILC) 2020. The studies, which evaluated safety, biochemical signs of liver damage, and hepatic fat, represent further progress in an emerging strategy for the treatment of fatty liver disease: the targeting of lipid metabolism. The potential for such treatments to address type 2 diabetes mellitus (T2DM) and obesity, as well as liver disease, makes them a focus for current research.

Non-alcoholic fatty liver disease (NAFLD) is estimated to affect approximately 25% of the global population and is the fastest growing liver disease globally,[1] with NASH putting patients at risk for complications such as hepatocellular carcinoma and cirrhosis. The reported prevalence of NASH varies widely, but estimates suggest that 1.5–6.5% of the general population has NASH and about one in five of these cases can progress to cirrhosis.[2] New epidemiological data also presented at DILC 2020 by Dr Zobair Younossi, President of Inova Medicine and Chairman of the Department of Medicine at Inova Fairfax Medical Campus, Falls Church VA, USA reported that NAFLD is now the second most common cause of liver-related deaths in the USA (26.3%), closely behind alcoholic liver disease (27.9%). Among individuals who died with NAFLD, the leading causes of death were liver-related (53.1%), cardiovascular disease (12.2%), and non-liver cancer (6.6%). In fact, cancer deaths were related to liver cancer (42.6%), lung cancer (8.5%), colorectal cancer (6.9%), pancreatic cancer (5.5%), and breast cancer (4.2%).

While there are currently no approved pharmacological options indicated for NASH, research has been focused on a wide range of mechanisms that underlie processes common to multiple pathologies, including lipid metabolism.[3] As NASH is estimated to be present in 37.3% of patients with T2DM,[4] receptors influencing lipid metabolism and inflammation have been a key area of focus. These include the farnesoid X receptor (FXR), which negatively regulates hepatic gluconeogenesis,[5] lipogenesis, and steatosis,[6] and the glucagon-like peptide-1 (GLP-1) receptor, which improves glucose control and reduces body weight by decreasing appetite, influencing hepatic lipid content and inflammation.[7]

Results on a novel FXR agonist, designated EDP-305, were presented at DILC 2020. In the Phase 2a ARGON-1 study, patients with fibrotic NASH without cirrhosis were randomized to placebo (n=24), EDP-305 1 mg (n=55), and EDP-305 2.5 mg (n=53) groups and treated for 12 weeks. The higher-dose EDP-305 group exhibited significant reductions vs placebo in ALT (-27.9 U/L; p=0.0495), fat percentage (-7.1%; p=0.0009; measured by magnetic resonance imaging-proton density fat fraction), gamma-glutamyl transferase (-49.4 U/L; p<0.0001), and C4 as a pharmacodynamic marker (-72%; p<0.001). High-density lipoprotein was also significantly reduced (-0.21 mmol/L; p<0.0001). Pruritus was the most common treatment-emergent AE, present in <5%, <10%, and 51% of subjects in the placebo, EDP-305 1 mg, and EDP-305 2.5 mg groups, respectively. This led to discontinuation in 1.8% and 20.8% of the EDP-305 1 mg and EDP-305 2.5 mg groups, respectively.

“This trial confirms that FXR agonism is a valuable therapeutic target in NASH with strong antisteatotic effects and the potential to reduce inflammatory injury to the liver”, said presenter Dr Vlad Ratziu, Professor of Hepatology at Sorbonne University and Pitié

Salpêtrière Hospital, Paris, France. “This highlights the need to conduct large and longer-term trials to show histological benefit at the dose that will minimize the side-effects of this class of drugs”.

The second study examined the first-in-class GLP-1/glucagon dual-receptor agonist, cotadutide. This Phase 2b study enrolled 834 overweight or obese patients with T2DM over 54 weeks of treatment; it was designed to assess the holistic metabolic effects of cotadutide and included an exploratory analysis of liver biomarkers. Patients were randomized to placebo, open-label once-daily liraglutide 1.8 mg, or once-daily subcutaneous cotadutide (100 µg, 200 µg, or 300 µg) for 54 weeks. At the end of treatment, significant reductions in body weight were observed at all cotadutide doses vs placebo ($p<0.001$) and cotadutide 300 µg vs liraglutide ($p=0.009$). Corresponding significant decreases in ALT were also observed for cotadutide 200 µg (-12 U/L; $p=0.009$) and 300 µg (-14.1; $p=0.003$) vs placebo, and cotadutide 300 µg vs liraglutide ($p=0.023$). Improvements in NAFLD fibrosis score (NFS) ($p=0.01$) and FIB-4 ($p=0.004$) with cotadutide 300 µg vs placebo further confirmed these results.

“We have demonstrated that cotadutide yielded greater reductions in ALT with similar weight loss to the GLP-1 receptor mono agonist liraglutide at 200 µg, and greater weight loss and ALT reductions at 300 µg in patients with T2DM”, said Dr Philip Ambery, Global Clinical Leader, Late CVRM at AstraZeneca, Gothenburg, Sweden, who presented the study. “The improvements seen in the NFS and FIB-4 are encouraging, and support the need for prospective clinical trials with cotadutide in patients with NASH. ”

“The epidemiological data confirm that NAFLD associated with dysmetabolism is becoming a major cause of liver disease, highlighting the importance of finding effective treatments for this condition”, said Professor Luca Valenti, an EASL Scientific Committee member from the University of Milan, Italy. “These clinical studies show that targeting FXR, GLP-1 and gastrointestinal hormone receptors are promising approaches for the treatment of NASH, which are worth to be further evaluated”.

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Session Details

Session title: NAFLD – Clinical except therapy

Date and time of session: Thursday 27 August 2020, 15.45–16.00

Presenter: Zobair Younossi

Abstract: Causes of death in patients with nonalcoholic fatty liver disease (NAFLD): data from national vital statistics system (NVSS)

Session title: NAFLD – Pharmacological therapy

Date and time of session: Friday 28 August 2020, 11.45–12.00

Presenter: Philip Ambery

Abstract: Effects of cotadutide on biomarkers of nonalcoholic steatohepatitis in overweight or obese subjects with type 2 diabetes mellitus: a 54-week analysis of a randomized phase 2b study

Session title: NAFLD – Pharmacological therapy

Date and time of session: Friday 28 August 2020, 12.15–12.30

Presenter: Vlad Ratziu

Abstract: EDP-305, a non-bile acid Farnesoid X receptor (FXR) agonist, showed statistically significant improvements in liver biochemistry and hepatic steatosis in the Phase 2a ARGON-1 study

Author disclosures

Zobair Younossi is a consultant to AbbVie, BMS, Genfit, Gilead, Intercept, Madrigal, Merck, Novo Nordisk, Quest Diagnostics, Siemens, Tern Pharmaceuticals, and Viking.

Philip Ambery is an employee and shareholder of AstraZeneca. He is also a Consultant Physician in Acute Medicine with Cambridge University Hospitals Trust, UK.

Vlad Ratziu is a consultant for Enanta and Intercept.

References

1. Younossi ZM, et al. Global epidemiology of non-alcoholic fatty liver disease - Meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology*. 2016;64(1):73–84.
2. Spengler EK, Loomba R. Recommendations for diagnosis, referral for liver biopsy, and treatment of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis. *Mayo Clinic Proceedings*. 2015;90(9):1233–46.
3. Oseini AM, Sanyal AJ. Therapies in non-alcoholic steatohepatitis (NASH). *Liver Int*. 2017;37(Suppl 1):97–103.
4. Younossi ZM, et al. The global epidemiology of NAFLD and NASH in patients with type 2 diabetes: A systematic review and meta-analysis. *J Hepatol*. 2019;71(4):793–801.
5. Hou Y, et al. Farnesoid X receptor: An important factor in blood glucose regulation. *Clin Chim Acta*. 2019;495:29–34.
6. Chávez-Talavera O, et al. Bile Acid Control of Metabolism and Inflammation in Obesity, Type 2 Diabetes, Dyslipidemia, and Nonalcoholic Fatty Liver Disease. *Gastroenterology*. 2017;152(7):1679–94.
7. Petit JM, Vergès B. GLP-1 receptor agonists in NAFLD. *Diabetes Metab*. 2017;43(Suppl 1):2S28–33.

PRESS RELEASE

EMBARGO: 00:01 CEST, THURSDAY, 27 AUGUST, 2020

Prioritizing patients using MELD-Na could reduce liver transplant waiting-list mortality in Europe

Digital ILC 2020: European study reports that prioritizing patients for liver transplantation using MELD-Na could reduce 90-day waiting-list mortality compared with current practice

EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER (EASL)

27 August 2020: Prioritizing patients for liver transplantation using the Model for End-stage Liver Disease Sodium (MELD-Na) score, instead of the more commonly used MELD score, could increase the chances of high-risk patients receiving a transplant and reduce the risk of dying while on the waiting list, according the results of a large study using data from the Eurotransplant network. Researchers from Leiden University Medical Center in the Netherlands evaluated more than 5,000 patients with chronic liver disease who had been allocated to the Eurotransplant liver waiting list using the MELD score, and found that more than one-quarter of those who died within 3 months of being listed might have received a transplant if the MELD-Na score had been used instead.

The MELD score, which estimates mortality risk for patients with end-stage liver disease using laboratory variables, has been used to prioritize patients on liver transplant lists for almost 20 years.1,2 Although MELD has been very successful in prioritizing patients,1 it does not accurately reflect the risk of death in patients with hyponatremia (low sodium levels), which is an important predictor of mortality in patients on liver transplant lists.3,4 The MELD-Na score, which includes serum sodium in the risk calculation, was adopted in the United States in 2016 for liver transplant prioritization,5 but is not yet used routinely across Europe.

To test whether the use of the MELD-Na score in the Eurotransplant region (which includes Austria, Belgium, Croatia, Germany, Hungary, Luxembourg, the Netherlands, and Slovenia) could improve outcomes, the Leiden team evaluated 5,223 patients who were allocated onto the Eurotransplant liver transplant waiting list between 2007 and 2018 using their MELD scores. These patients were followed from their first listing to the time of delisting or until 90 days after listing. As part of the study, each patient was reclassified retrospectively based on their MELD-Na score, allowing an estimation of the number of lives saved if MELD-Na allocation had been used.

According to Dr Ben Goudsmit from Leiden University Medical Center, who presented the study results at this year's Digital International Liver Congress™, a large proportion (40%) of patients on the transplant waiting list had hyponatremia, and these patients had a three-fold increased risk of dying within 90 days of being listed.

'We also found that, if the MELD-Na score had been used to prioritize patients instead of the MELD score, 26.3% of those who died within 90 days would have had a significantly higher chance of receiving a liver transplant', he said. 'This equates to a 4.9% reduction in 90-day waiting-list mortality'.

The research team believes that, since there is a shortage of liver grafts and the prevalence of cirrhosis is increasing globally, better prediction of mortality and improved prioritization for liver transplantation are becoming increasingly important. 'We believe that MELD-Na-based allocation would help to prioritize patients on European liver transplant waiting lists and reduce the number of patients who die before they get the chance of receiving this life-saving treatment'.

'The MELD score was a breakthrough in the field of liver transplantation, as it ensured equity in patients assessed and listed for a transplant. Over the years, it became apparent

that the addition of Na to the original equation improved the classification of patients, and the MELD-Na was subsequently adopted in the US in 2016', explained Professor Emmanuel Tsochatzis of the Royal Free Hospital and University College London, UK, and an EASL Governing Board member. 'This study is an important step in introducing MELD-Na in the European liver transplant programs, as it demonstrated an almost 5% improvement in 90-day waiting list mortality'.

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Session Details

Session title: General session I

Date and time of session: Thursday 27 August 2020, 14.15–14.30

Presenter: Ben Goudsmit

Abstract: Validation of the model for end-stage liver disease sodium score for the Eurotransplant region

Author Disclosures

Ben Goudsmit and the study authors have no relevant disclosures.

References

1. Brock GN, et al. Use of rapid Model for End-Stage Liver Disease (MELD) increases for liver transplant registrant prioritization after MELD-Na and Share 35, an evaluation using data from the United Network for Organ Sharing. *PLoS One*. 2019;14(10):e0223053.
2. Cholongitas E, Burroughs AK. The evolution in the prioritization for liver transplantation. *Ann Gastroenterol*. 2012;25(1):6–13.
3. Biggins SW, et al. Serum sodium predicts mortality in patients listed for liver transplantation. *Hepatology*. 2005;41(1):32–9.
4. Kim WR, et al. Hyponatremia and mortality among patients on the liver-transplant waiting list. *N Engl J Med*. 2008;359(10):1018–26.
5. United Network for Organ Sharing. OPTN/UNOS Liver and Intestinal Organ Transplantation Committee. Report to the board of directors. Richmond, Virginia. 2014 Jun. Available from: https://optn.transplant.hrsa.gov/media/1834/liver_boardreport_20140702.pdf. Accessed 17 February 2020.

PRESS RELEASE

EMBARGO: 00:01 CEST, THURSDAY, 27 AUGUST, 2020

Changes in gut microbiota can significantly impact alcohol-related liver disease and cancer risk

Digital ILC 2020: Studies evaluating fecal microbial transplant and inflammatory signalling highlight the significance of gut microflora in alcohol-related liver disease and hepatocarcinogenesis

EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER (EASL)

27 August 2020: The importance of gut microbiota in alcohol-related liver disease and liver cancer has been demonstrated in two studies, presented at The Digital International Liver Congress™ 2020. The key role of microbial biodiversity in the gut was highlighted in a study of fecal microbial transplant, with the technique showing promise as an intervention to improve some aspects of alcohol-related liver disease. A second study used a mouse model to associate changes in gut microbiota with the action of key signalling molecules, mediating the risk of hepatocarcinogenesis.

In recent years, imbalances in gut microbiota, or dysbiosis, have been implicated as contributing to alcoholic liver disease.[1] In cases of chronic alcohol use, reactive oxygen species produced by alcohol metabolism can lead to chronic intestinal inflammation, which in turn can increase gut permeability and alter microbiota composition. This includes expansion of inflammation-associated bacteria such as *Proteobacteria*, and reduction of protective species such as *Faecalibacterium*.[1–3] Increased gut permeability is believed to lead to translocation of gut bacterial DNA and endotoxins to the liver.[4] The latter, in particular, are thought to induce pro-inflammatory toll-like receptor 4 (TLR4) signalling pathways that are associated with hepatocarcinogenesis.[5]

The importance of gut microbiota raises the possibility of exploiting its manipulation to improve patient outcomes. The first study tested whether fecal microbial transplant (FMT) – the transfer of fecal bacteria from a healthy individual to a patient – could reduce cravings for alcohol as the first step for use in subsequent larger trials. In a pilot, double-blind, placebo-controlled, randomized clinical trial, 20 patients with alcohol use disorder (AUD) and liver cirrhosis, who had tried several options to quit alcohol unsuccessfully, were given FMT or placebo, with FMT shown to reduce alcohol cravings as well as total and psychosocial sickness impact profile at Day 15 post-treatment. A corresponding significant increase in microbiota diversity was seen in FMT patients compared with baseline (p=0.02), including a higher relative abundance of *Odoribacter*. *Alistipes* and *Roseburia* were also more abundant in patients given FMT compared with placebo at Day 15.

'FMT was safe and shown to have an impact on reducing short-term alcohol cravings and improving psychosocial quality of life in patients with cirrhosis and AUD', added study presenter Dr Jasmohan S Bajaj of McGuire VA Medical Center, USA. 'The relative abundance of short-chain fatty acid-producing bacteria identified in patients with higher diversity after FMT demonstrates that altering the gut–brain axis is a potential avenue to alleviating AUD in those with cirrhosis'.

A second study explored how gut microbiota may affect the process of developing hepatocellular carcinoma, using mice that have been genetically engineered to develop steatohepatitis (NEMO$^{\Delta hepa}$ mice). By crossing these mice with others that have had other genes involved in the inflammatory response to bacteria inactivated, and then altering the gut microbial balance with broad-spectrum antibiotics, the research team showed that knocking out the NLRP6 receptor (a key mediator of colonic homeostasis that can cause intestinal dysbiosis if deficient[6]) leads to more severe steatohepatitis and a higher tumour burden. The degree of intestinal barrier permeability was highly correlated with tumour burden as well as several indicators of inflammation in the liver. Crucially, this immune

phenotype could be transferred to other mice by FMT, provided they had functional TLR4 signalling, and could be reversed if the transplanted microbiota were depleted with broad-spectrum antibiotics.

'Strikingly, we also found that replacing depleted *Akkermansia muciniphila* bacteria in the guts of these mice helped ameliorate their inflammation and steatohepatitis', said Dr Kai Markus Schneider of University Hospital RWTH Aachen, Germany. 'This knowledge of how short-term changes to microbiota reshape the hepatic tumour microenvironment has the potential to reveal new therapeutic options for cancer prevention and therapy'.

'The understanding of interactions between the human and microbiome genome (metagenome) in health and disease has represented one of the major areas of progress in the last few years', said Professor Luca Valenti, an EASL Scientific Committee member from the University of Milan, Italy. 'These studies lay the groundwork for exploiting this new knowledge for the treatment of liver disease'.

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Session Details

Session title: General session I

Date and time of session: Thursday 27 August 2020,14.00–14.15

Presenter: Kai Markus Schneider

Abstract: Gut microbiota drives hepatocarcinogenesis by promoting TLR4-dependent expansion of monocytic myeloid-derived suppressor cells

Session title: Alcohol-associated liver disease

Date and time of session: Thursday 27 August 2020, 11.30–11.45

Presenter: Jasmohan S Bajaj

Abstract: Fecal microbial transplant reduces short-term cravings, improves quality of life and microbial diversity in cirrhosis and alcohol use disorder: a randomized, placebo-controlled, clinical trial

Author Disclosures

Jasmohan S Bajaj and Kai Markus Schneider have no relevant disclosures.

References

1. Meroni M, et al. Alcohol or gut microbiota: who is the guilty? *Int J Mol Sci.* 2019;20(18):4568.
2. Engen, PA, et al. The gastrointestinal microbiome: alcohol effects on the composition of intestinal microbiota. *Alcohol Res.* 2015;37(2):223–36.
3. Bjørkhaug ST, et al. Characterization of gut microbiota composition and functions in patients with chronic alcohol overconsumption. *Gut Microbes.* 2019;10(6):663–75.
4. Li F, et al. Microbiome dysbiosis and alcoholic liver disease. *Liver Res.* 2019;3(3–4):218–26.
5. Wan MLY, El-Nezami H. Targeting gut microbiota in hepatocellular carcinoma: probiotics as a novel therapy. *Hepatobiliary Surg Nutr.* 2018;7(1):11–20.
6. Levy M, et al. Microbiota-modulated metabolites shape the intestinal microenvironment by regulating NLRP6 inflammasome signalling. *Cell.* 2015;163(6):1428–43.

PRESS RELEASE

EMBARGO: 00:01 CEST, THURSDAY, 27 AUGUST, 2020

Bezafibrate add-on treatment increases transplant-free survival in primary biliary cholangitis

Digital ILC 2020: Large Japanese study reports that the combination of bezafibrate plus ursodeoxycholic acid (UDCA) improves liver transplant-free survival compared with no treatment or UDCA monotherapy in patients with primary biliary cholangitis

EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER (EASL)

27 August 2020: The combination of bezafibrate and ursodeoxycholic acid (UDCA) has been shown to increase transplant-free survival compared with no treatment or UDCA monotherapy in a Japanese cohort study involving a large number of patients with primary biliary cholangitis (PBC). The study, which was reported at the Digital International Liver Congress™ (DILC) 2020, adds to the growing body of evidence suggesting that the addition of bezafibrate to UDCA therapy improves both biochemical markers and long-term outcomes in PBC, especially in patients with an inadequate response to UDCA.[1–3]

PBC is an immune-mediated liver disease that is characterized by the development of serum autoantibodies, inflammation, the destruction of small intrahepatic bile ducts, progressive cholestasis, and a slow progression towards cirrhosis and liver failure.[1,2] UDCA is the recommended first-line pharmacological treatment for PBC in Europe.[4] However, around 20% of patients show an inadequate response to UDCA,[5] and these patients are at greater risk of hepatic complications and more likely to need liver transplantation than treatment responders.[5,6]

Bezafibrate is a hypolipidaemic fibrate that is currently approved for the treatment of PBC in France.[2] It has been used in Japan as a second-line treatment for patients with PBC and an incomplete response to UDCA for more than a decade,[3] enabling an assessment of its long-term efficacy as a combination treatment.

The study, presented at the DILC 2020, was a retrospective analysis of 8,180 PBC patients of whom 6,087 (74%) received UDCA monotherapy, 943 (12%) received a combination of UDCA and bezafibrate, and 1,133 (14%) received no treatment; the remaining 17 patients received bezafibrate monotherapy. Patients treated with UDCA monotherapy had a significantly lower risk of all-cause death or liver transplantation than those receiving no treatment; the adjusted hazard ratio (aHR) was 0.55 (95% confidence interval [CI] 0.47, 0.65; p<0.0001). The addition of bezafibrate to UDCA conferred a further risk reduction compared with UDCA monotherapy, with an aHR of 0.23 (95% CI 0.15, 0.35; p<0.0001). Results were similar when considering a combined outcome of liver-related death or liver transplant.

“Ideally, the long-term effectiveness of UDCA and bezafibrate should be assessed in prospective, randomized, placebo-controlled studies”, said Dr Atsushi Tanaka from the Teikyo University School of Medicine in Tokyo, Japan, who presented the study findings. “This is challenging in Japan because bezafibrate is a standard-of-care second-line treatment”.

“However, this study evaluated a large nationwide cohort of PBC patients, and the addition of bezafibrate to UDCA produced enhanced long-term benefits, markedly reducing the risk of all-cause death or liver transplantation compared with UDCA treatment alone. As response to UDCA can now be anticipated from pre-treatment features, a new treatment approach may be to start bezafibrate combination therapy immediately in patients with a predicted poor response to UDCA”.

"Prospective, randomized, placebo-controlled trials of adequate size and duration are a golden standard to demonstrate the efficacy of novel therapeutic interventions in diseases for which treatment options are limited", said Professor Ulrich Beuers of the Tytgat Institute for Liver and Intestinal Research in Amsterdam, The Netherlands, and an EASL Governing Board member. "Retrospective analyses can also lead to enormous knowledge gain when carefully performed. In PBC, UDCA (13–15 mg/kg/day) is the standard of care for all patients. Japanese clinicians and researchers were the first to combine UDCA with bezafibrate treatment in patients who did not respond adequately to UDCA alone. The retrospective analysis presented by Professor Tanaka, representing a large group of Japanese hepatologists, summarizes the Japanese long-term experience with UDCA and bezafibrate in a cohort of more than 8000 PBC patients. This report, together with well-designed prospective studies, will have major impact for the future management of PBC worldwide and deserves deep appreciation for the efforts of our Japanese colleagues".

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Session Details

Session title: General session I

Date and time of session: Thursday 27 August 2020, 13.15–13.30

Presenter: Atsushi Tanaka

Abstract: Bezafibrate add-on therapy improves liver transplantation-free survival in patients with primary biliary cholangitis: a Japanese nationwide cohort study

Author Disclosures

Atsushi Tanaka reports receiving consultant fees from EA Pharma, Gilead Sciences, and GlaxoSmithKline. Among the study co-authors: Bettina Hansen has received unrestricted grants and consultant fees from Albireo, Calliditas, Cymabay, Intercept, and Mirum, and consultant fees from ChemoMab and Genfi; Olivier Chazouillères has received grant support from Aptalis, fees for teaching from Mayoly Spindler, consulting fees from Genfit, and fees for teaching and consulting fees from Intercept; and Christophe Corpechot has received grants from Arrow and Intercept France, consulting fees from GenKyoTex, Intercept France, and Inventiva Pharma, and fees for teaching from GlaxoSmithKline France and Intercept France. No other potential conflicts of interest relevant to this study are reported.

References

1. Corpechot C, et al. A placebo-controlled trial of bezafibrate in primary biliary cholangitis. *N Engl J Med*. 2018;378(23):2171–81.
2. Agrawal R, et al. Effectiveness of bezafibrate and ursodeoxycholic acid in patients with primary biliary cholangitis: a meta-analysis of randomized controlled trials. *Ann Gastroenterol*. 2019;32(5):489–97.
3. Honda A, et al. Bezafibrate improves GLOBE and UK-PBC scores and long-term outcomes in patients with primary biliary cholangitis. *Hepatology*. 2019;70(6):2035–46.
4. European Association for the Study of the Liver (EASL). EASL Clinical Practice Guidelines: The diagnosis and management of patients with primary biliary cholangitis. *J Hepatol*. 2017;67(1):145–72.
5. Harms MH, et al. Ursodeoxycholic acid therapy and liver transplant-free survival in patients with primary biliary cholangitis. *J Hepatol*. 2019;71(2):357–65.
6. Harms MH, et al. Major hepatic complications in ursodeoxycholic acid-treated patients with primary biliary cholangitis: risk factors and time trends in incidence and outcome. *Am J Gastroenterol*. 2018;113(2):254–64.

PRESS RELEASE

EMBARGO: 00:01 CEST, THURSDAY, 27 AUGUST, 2020

New models help predict hepatocellular carcinoma (HCC) after successful hepatitis C virus (HCV) treatment

Digital ILC 2020: European scientists develop new predictive models for HCC in patients with chronic HCV after a sustained virological response to direct-acting antiviral therapy

EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER (EASL)

27 August 2020: Predicting who may go on to develop hepatocellular carcinoma (HCC) after successful treatment for chronic hepatitis C virus (HCV) infection may now be easier thanks to the work of two independent research teams from France and Egypt. The studies, presented at The Digital International Liver Congress™ (DILC) 2020, included cohorts of patients with chronic HCV infection who achieved a sustained virological response (SVR) to direct-acting antiviral (DAA) therapy and all used readily available clinical parameters to find those at lowest and highest risk of developing HCC in the future. This, they say, could help to individualize HCC surveillance and detect HCC after HCV is cured as early as possible.

DAA-based treatment can achieve an SVR in more than 95% of patients with chronic HCV infection.1 Despite viral eradication, however, patients with chronic HCV continue to have a residual risk of HCC, especially those with severe underlying liver disease and/or comorbidities.2,3 Risk factors and prediction models for HCC are better understood in HCV-infected patients prior to eradication, but these have not yet been established in patients who achieve an SVR with DAA therapy.

Important statistical work was presented by the French group using data from subjects with biopsy-proven compensated cirrhosis from the French ANRS CirVir prospective cohort of patients. They aimed to identify specific longitudinal profiles associated with patients likely to develop HCC after HCV eradication according to serum alpha fetoprotein (AFP) and routine serum biomarkers (gamma-glutamyl transferase [GGT], alanine aminotransferase [ALT] and aspartate aminotransferase [AST]). In this cohort, a total of 142/717 patients with HCV at baseline and 47/413 who achieved SVR developed HCC, over a median follow-up period of 74.2 months. Among those who achieved SVR, the researchers identified two distinct types of patients at an elevated risk of developing HCC: one cluster with elevated serum parameters (n=95; 13.7% HCC incidence) and one with impaired liver function (n=109; 15.6% HCC incidence). A third patient cluster, whose AFP and biochemical marker levels tended towards normalization, had a lower incidence of HCC (n=228; 7.5% incidence). Examining the pre-SVR population also showed clusters of patients with either a globally worsening liver function (n=198; 26.8% incidence) or a trajectory of increasing levels of AFP and serum biomarkers (n=190; 25.3% incidence). Again, a third cluster of biomarker levels that were favourable and stable overall had lower rates of HCC (n=329; 12.5% incidence; $p<0.0001$ vs the two other clusters).

“These analyses, based on novel statistical methods, suggest HCC surveillance can be refined and improved in order to tailor patient management to achieve optimum outcomes and increase cost-effectiveness,” explained presenter and study lead Dr Pierre Nahon of Assistance Publique – Hôpitaux de Paris, Hôpital Jean Verdier, France.

In practical terms, better knowledge of who is most at risk of developing HCC could have an important impact on how screening programmes are implemented. Bringing us close to this goal, both the research team from France and another from Egypt presented potential scoring systems to achieve this goal. The ANRS C022 HEPATHER study used data from a large hepatitis B or C cohort, selecting 7,752 individuals with chronic HCV who were HCC-free, had no detectable hepatitis B virus antigens, and had achieved an SVR 12 weeks after

DAA treatment. Individuals were followed for a median of 2.2 years (interquartile range 1.2–3.3 years), during which 220 (2.8%) developed HCC. Eight independent variables were found to be associated with HCC occurrence: male gender, age >64 years at SVR, advanced liver fibrosis (fibrosis scores of 3 or 4 [F3 or F4]), HCV genotype 3, presence of oesophageal varices, baseline serum AFP >5.5 ng/ml, AST to platelet ratio index (APRI) >2 at end of treatment, and previous interferon-based regimen(s) with or without ribavirin. The team then developed an HCC risk score using these variables, enabling stratification of patients into three groups according to HCC risk level (high, intermediate, low) at 1 and 3 years post-treatment. The HCC risk score was found to have a good predictive performance; most individuals evaluated (76.5%) were in the low-risk group at 3 years, with an HCC incidence of <1.5%.

“These results may allow us to target our surveillance towards those at highest risk during the first 3 years after SVR,” said Professor Nathalie Ganne-Carrié, also from Assistance Publique – Hôpitaux de Paris, Hôpital Jean Verdier, France, who presented the study findings at ILC 2020.

Working to the same goal, researchers from the Egyptian Liver Research Institute and Hospital undertook a prospective study in which 2,326 patients with chronic HCV infection and advanced hepatic fibrosis or liver cirrhosis (F3 or F4) who achieved an SVR were followed for an average of 24 months (range 12–45 months). One hundred and nine patients (4.7%) developed HCC during the follow-up period. Risk factors for HCC were similar to those observed by the French group, although a smaller number of factors were identified in the Egyptian study: age, sex, serum albumin, AFP, and pretreatment fibrosis stage. Using these variables, a simple scoring system was then developed, which stratified patients into low-, medium- and high-risk groups with a good predictive accuracy. The 2-year cumulative incidence of HCC in these groups was 2.0%, 4.5%, and 10.3%, respectively. If validated, say the researchers, the simple scoring system could help to individualize HCC screening of HCV-infected patients after successful DAA treatment.

“These three studies reflect the complexity of understanding hepatocarcinogenesis and refute the idea that cure of HCV is equal to eliminating the risk of liver cancer,” said Dr Jordi Bruix, of the Hospital Clinic of Barcelona, Spain, and EASL Governing Board member. “The proposed scores potentially represent a useful clinical tool to help inform patients about the risk of developing HCC after HCV is cured. These data also reinforce the importance of implementing HCC screening programmes in DAA-treated patients and the need to reinforce research efforts to identify the causes of liver cancer development despite cure of HCV.”

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Session Details

Session title: General Session II

Date and time of session: Friday 28 August 2020, 14.36–14.51

Presenters: Pierre Nahon, France

Abstract: Profiling of routine serum parameters and AFP evolution in cirrhosis following HCV eradication for stratification of HCC risk: a trajectory clustering analysis from the ANRS CO12 CirVir cohort

Session title: HCV Long-Term Management

Date and time of session: Thursday 27 August 2020, 16.15–16.45

Presenters: Nathalie Ganne-Carrié, France, and Gamal Shiha, Egypt

Abstracts: Predictive models for hepatocellular carcinoma (HCC) occurrence in patients with chronic hepatitis C and sustained virological response (SVR) achieved with direct acting anti-viral (DAA) included in the ANRS C022 HEPATHER cohort (AS154) and A simple score

for HCC risk stratification in CHC patients with cirrhosis or advanced hepatic fibrosis who achieved SVR following DAA therapy (AS155)

Author disclosures

Pierre Nahon has received fees or funding from AbbVie, AstraZeneca, Bayer, BMS, Eisai, Gilead, MSD and Roche

Nathalie Ganne-Carrié has received invitations to speak at medical meetings from AbbVie, Bayer, Gilead, Ipsen, and consulting fees from Bayer, Gilead and Shionogi

Gamal Shiha has no relevant disclosures

References

1. Su F, Ioannou GN. Hepatocellular carcinoma risk after direct-acting antiviral therapy. *Clin Liver Dis (Hoboken)*. 2019;13(1):6–12.
2. El-Serag HB, et al. Risk of hepatocellular carcinoma after sustained virological response in veterans with hepatitis C virus infection. *Hepatology*. 2016;64(1):130–7.
3. Adhoute X, et al. Impact of direct-acting antiviral agents on the risk for hepatocellular carcinoma. *Transl Gastroenterol Hepatol*. 2017;2:110.

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BACKGROUND INFORMATION

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Track descriptions as published on the ILC website, as of 15 August 2020

Cirrhosis and Complications

As our knowledge of liver physiology expands, so too does our understanding of the critical role played by the vascular system in both the development and progression of liver disease. While liver sinusoidal changes are known to affect disease progression, they also have a knock-on effect, disrupting circulation in the rest of the body. The Cirrhosis and Complications track at Digital ILC 2020 will explore the complex relationship between vascular changes and liver cirrhosis, and will highlight the management of portal hypertension.

In its quest to beat liver disease, EASL efforts include devoting a full track to this topic at its events, supporting consortia and collaborations aimed at advancing pertinent research, and having published the EASL Clinical Practice Guidelines on the Management of Decompensated Cirrhosis, which are consulted worldwide.

The Cirrhosis and Complications programme will allow you to learn, share, and interact, due to its engaging structure containing poster tours, abstract sessions, interactive sessions, industry symposia, meet the experts, and wrap up sessions.

General Hepatology

The General Hepatology track will explore the most important advances relevant to healthcare professionals and scientists with an interest in liver disease. A full track programme will focus on the very latest developments in liver disease management.

Looking at the system level, Digital ILC 2020 will also address the importance of bringing hepatology into the primary care setting, the role of society in improving general liver health, and the pros and cons of screening in the general population.

The track sessions will provide updates on immunometabolism, non-invasive assessment of liver disease/health, emerging biological markers and targets, plus a dedicated session on COVID-19. There will be a focus on managing liver disease in vulnerable groups, including pregnant women and adolescents.

Immune-mediated and cholestatic disease

Significant unmet needs remain for patients with immune-mediated and cholestatic liver diseases, compounded by a broad disease manifestation spanning several body systems and a multifaceted aetiology that complicates the search for new drug targets. With a dedicated track for this challenging area, Digital ILC 2020 brings the clinical and scientific communities together in a showcase of the latest knowledge and experience from leading experts.

Cholestatic and immune-mediated liver diseases are currently incurable. Treatment options allow a degree of symptomatic control, but do not significantly halt disease progression. With much still to learn about the genetic and cellular processes that underlay cholestasis, and complex aetiology that affects management approaches,

Digital ILC 2020 will be a vital platform for hepatologists, scientists, and other healthcare professionals to share their experience in this area, hear about the latest breakthroughs, and take the next steps in improving the short- and long-term health outcomes of their patients.

The Immune-Mediated and Cholestatic Diseases track programme will allow you to learn, share, and interact, due to its engaging structure: with poster tours, abstract sessions, interactive sessions, industry symposia, meet the experts, and wrap up sessions.

Liver Tumours

The landscape of liver cancer is changing. With recent progress in the treatment and elimination of the hepatitis C virus (HCV), liver tumours caused by viral hepatitis are becoming less common.

Yet a worsening obesity epidemic is shifting liver cancer towards a greater prevalence of metabolic disease-related tumours. Improving our understanding of the mechanisms of liver cancer and developing new therapies remains crucial.

The Liver Tumours track at Digital ILC 2020 will showcase the latest advances and equip clinicians for the coming challenges in the field of liver cancer.

Metabolism, Alcohol and Toxicity

Globally, 1 in 4 people are living with fatty liver disease, with obesity, alcohol consumption, and sedentary lifestyles as key contributors.

EASL has been actively working to beat liver disease, including NAFLD & NASH, through its schools and key event, the NAFLD Summit. EASL has also developed a Policy Statement on the measures required to prevent and treat this common progressive condition. Globally, 1 in 4 people are living with fatty liver disease, with obesity, alcohol consumption, and sedentary lifestyle behaviours as key contributors.

Fatty liver is a silent but deadly epidemic with many people remaining asymptomatic well into the advanced stages of disease. The development of new therapies, the use of biomarkers in NAFLD, and how microbiota and genes can modulate alcohol-related liver disease (ALD) are current key research questions that will be addressed during Digital ILC 2020.

In the Metabolism, Alcohol and Toxicity track at Digital ILC 2020, world-renowned experts will examine the metabolic factors associated with liver disease, and how they interact with genetics, inflammation, and the gut–liver axis. Follow this track to learn about the interaction of all these factors and highlight promising new research in screening, monitoring, and treatment.

Viral Hepatitis

The curative potential of direct-acting antivirals (DAAs) for hepatitis C virus (HCV) infection have transformed hepatology in recent years. However, the challenge of identifying more people living with HCV remains, and further progress is needed with other forms of viral hepatitis. The Viral Hepatitis track at Digital ILC 2020

updates on our progress towards HCV elimination and highlights the latest breakthroughs in finding a cure for hepatitis B.

The World Health Organization has called for elimination of viral hepatitis as a global public health threat by the year 2030 and Digital ILC 2020 will provide a platform for leading experts to discuss the remaining obstacles to HCV elimination and review the upcoming treatments and new insights for other forms of viral hepatitis.

The Viral Hepatitis track programme will allow you to learn, share, and interact, due to its engaging structure containing poster tours, abstract sessions, interactive sessions, industry symposia, meet the experts, and wrap up sessions.

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