Congress Review

Review of The Digital International Liver Congress (ILC) 2020

Location: The Digital ILC 2020

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LONDON, UK, is considered to be one of the world's most influential cities, with a significant impact on arts, commerce, and finance, but also on education, healthcare, and research. The city was the home of Robert Hooke, who was the first to visualise a micro-organism under a microscope and coined the term 'cell' in 1665; it also houses St Mary's Hospital where Sir Alexander Fleming first discovered penicillin in 1928. The city has served as a major global hub for innovation and scientific advancements and continually attracts experts across various disciplines. These qualities, against a backdrop of London's historic scenery, has made the UK's capital a popular destination to host world-leading congresses such as the International Liver Congress (ILC), which attracted 8,560 participants from 117 countries in 2019.

2020 marks the 55th European Association for the Study of the Liver (EASL) ILC; however, "2020 has been a year like no other in recent memory, and coronavirus disease (COVID-19) continues to be a major societal challenge," reflected Prof Newsome, EASL Secretary General, host of this year's ILC Opening Ceremony. Although many advances have been made during the global COVID-19 pandemic, Prof Newsome underlined an accompanying consequence: the widespread cancellation of face-to-face congresses, including the flagship ILC, which was due to be held in London in April. However, this did not encourage EASL to cancel ILC. "Necessity is the mother of invention," Prof Newsome confidently stated as he welcomed everyone to the first ever virtual 3-day event: The Digital ILC. In the live broadcast, he continued to thank the delegates and EASL's industry partners for their continued support throughout these difficult times. This appreciation was extended to the efforts and innovation of the EASL Governing Board, EASL committees, and the EASL Office for their "herculean" efforts to organise the digital congress in such a short time frame.

The Digital ILC offered a plethora of stimulating content, both live and on-demand, to explore new ways to engage with the community and reach a global

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audience. Prof Newsome asserted: "We have worked hard to ensure that this year's Digital ILC is an immersive experience, to learn all about the latest in science, education, and advances in liver disease therapy." A key component distinguishing The Digital ILC was the EASL Studio: the main meeting room of the EASL Governing Board and the Editorial Team in Geneva, Switzerland, was transformed into a live hub and platform where top experts of the field could converse, recap, and disseminate the events of the day.

Comprising hundreds of hours of content, including >90 sessions, >200 fully live posters, >1,500 ePosters with video presentations, and 46 abstracts with live question and answer sessions, The Digital ILC was a fascinating experience. The content covered all liver specialities, categorised into six disease tracks: general hepatology; metabolism, alcoholism, and toxicity; liver tumours; viral hepatitis; cirrhosis and complications; and immune-mediated and cholestatic diseases.

The EASL Community Hub featured live virtual booths for networking and opportunities to learn from, or participate in, EASL initiatives on science, education, and advocacy. It was impossible to miss the latest news, videos, and updates as EASL's Newsroom was always up to date. After a long day at the digital congress, the EASL Lounge provided a space to relax and network; source new, healthy recipes; take a virtual trip through London; or, for those that needed to get blood circulating after sitting all day, try the 15-minute live yoga sessions.

Jumping between the live format and prerecorded videos, the Opening Ceremony included special guests Honorary President Prof Jaime Bosch; Michelle Clayton, Head of EASL Nurses and Allied Health Professionals Task Force; and Martine Walmsley, Chair of Trustees for Primary Sclerosing Cholangitis Support. The ceremony also paid special tribute to valued members of the community, including the recent passing of Prof Rodger Williams, "a true pioneer in liver disease and an inspiration to the world of hepatology," who was due to receive a Lifetime Achievement Award at the ILC in London. Awards presented at The Digital ILC included the EASL Emerging Leaders Award, dedicated to young, distinguished fellows <40 years old and active EASL members who have achieved important accomplishments in liver research; the 2020 awards were presented to Dr Thomas Reiberger and Dr Prakash Ramachandran. The winners of this year's EASL Recognition Award were Prof Giovanna Fattovich and Prof Patrick Marcellin, and the International Recognition Awards were presented to Prof Michael Trauner and Prof James L. Boyer.

The Digital ILC provided the audience with an abundance of breakthroughs in the field. We have compiled some of this trailblazing research in the following pages, with topics ranging from the function of the enzyme monoacylglycerol lipase in liver regeneration, to new guidelines on hepatic encephalopathy in transjugular intrahepatic portosystemic shunt use, and the hidden population living with advanced liver disease. We have also recruited some of the presenting abstract authors to write a summary of their research; these provide a first-hand account of the progress made in hepatitis C testing as part of the Hepatitis C Elimination Programme in Georgia, the diagnostic and prognostic role of presepsin in patients with cirrhosis and bacterial infection, and much more.

During the Opening Ceremony, co-host Prof Thomas Berg, EASL Vice Secretary, hoped that the congress would have "the maximum interaction, something which we all have missed over the past 6 months"; after the 3-day official event, the congress continued with a series of Digital Takeaways, providing a series of open-access expert discussions and debates, and eight 30-minute thematic webcasts throughout September and October. This spirit of supporting engagement, embracing digital connectedness, and maximising opportunities to share in liver research was on brilliant display throughout the congress, and we look forward to the continuation of this spirit in next year's ILC, planned for Amsterdam, the Netherlands, in June.

ILC 2020 REVIEWED →

The Function of Monoacylglycerol Lipase in Liver Regeneration

REGENERATIVE properties of the enzyme monoacylglycerol lipase (MAGL) were highlighted in new data presented at The Digital ILC as a press release on 28th August and may pave the way forward towards understanding the mechanisms of liver regeneration.

Currently, the only treatment for end-stage liver disease or acute liver failure is liver transplantation. However, obtaining donors is extremely challenging and therefore the capability of the liver to regenerate and repair itself has received increased attention, in the hope of finding alternatives to transplantation.

The proinflammatory enzyme MAGL reprogrammes lipid metabolism by converting monoacylglycerols into free fatty acids. Previously, both genetic (*MAGL-/-*) and pharmacological (MJN110 inhibitor) invalidation have benn shown to reduce inflammation and slow fibrosis progression in mice. In their study, the researchers assessed whether inhibition of MAGL could affect liver regeneration and found that MAGL-invalidated mice with liver damage had impaired liver regeneration compared with wild-type counterparts. Furthermore, MAGL deficiency was linked to a decreased production of inflammatory mediators (PGE2) and reduced mRNA expression of TGF-α, IL-17, and hepatocyte growth factor after liver injury. Impairment in liver regeneration was also seen in mice where MAGL was specifically inactivated in hepatocytes or myeloid cells.

Dr Manon Allaire, Center for Inflammation Research, Paris, France, summarised: "Inhibition of MAGL is associated with compromised liver regeneration, that results both from a direct effect on hepatocytes and an indirect effect on macrophages. Thus, while being profibrogenic, MAGL displays proregenerative capacities in the liver." Ideally, therapies for end-stage liver disease or acute liver failure would both target fibrosis and promote liver regeneration, and the data presented here highlighted that MAGL could be a therapeutic target for chronic liver disease and potentially other therapeutic lipid metabolism targets.

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Fecal Microbial Transplant for Treatment of Alcoholic Liver Disease and Hepatocarcinogenesis

TECHNIQUES highlighting the significant effect of microbial biodiversity in the gut may be effective in improving aspects of alcoholic liver disease. The fecal microbial transplant could serve as an intervention to alleviate adverse symptoms of the disease. This is according to the results of two new studies which were presented as part of a press release dated 27th August 2020 at The Digital ILC 2020.

This first study was a pilot, double-blind, placebo-controlled, randomised clinical trial that investigated cravings for alcohol following a fecal microbial transplant after fecal bacteria from a healthy person was transferred to a patient with alcohol use disorder and liver cirrhosis. The patients, who had made previous attempts to overcome their disorder but were unsuccessful in abstaining, were given a fecal microbial transplant or placebo. At Day 15 post-treatment, results from the 20 patients showed fecal microbial transplant reduced alcohol cravings and the psychosocial impact profile. Researchers found an abundance of microbiota diversity in patients who had a fecal microbial transplant including higher levels of *Odoribacter, Alistipes*, and *Roseburia*, compared to the placebo group at Day 15.

The second study presented as part of the same press release investigated the effect of gut microbiota on hepatocellular carcinoma in a study which incorporated mice that had been genetically engineered to develop steatohepatitis. The researchers crossed these mice with another group that had different gene expressions in their inflammatory responses and then treated them with antibiotics. The team showed that knocking out the NLRP6 receptor, a mediator of colonic homeostasis, led to more severe steatohepatitis and a higher tumour burden. The degree of intestinal barrier permeability was highly correlated with tumour burden and fecal microbial transplant was shown to successfully transfer this immune phenotype to other mice by fecal microbial transplant in a reversible process if the transplanted microbiota were depleted with broad-spectrum antibiotics. Dr Kai Markus Schneider, University Hospital RWTH Aachen, Aachen, Germany, commented on the therapeutic potential of these results: "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."

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New Guidelines on Hepatic Encephalopathy in Transjugular Intrahepatic Portosystemic Shunt Use

COMPLICATIONS of transjugular intrahepatic portosystemic shunt (TIPS) in patients with high-risk liver cirrhosis and acute variceal bleeding (AVB) have deterred attending physicians from performing the procedure, especially in patients with existing hepatic encephalopathy (HE). Through international collaboration, new evidence has been obtained to support the use of TIPS in this population of patients, according to a study presented at The Digital ILC 2020 and a press release dated 28th August 2020.

HE impairs brain function through the accumulation of toxic molecules in the bloodstream as a result of the liver being unable to remove them, and is a potential complication of TIPS, a therapeutic procedure for portal hypertension which has the life-threatening complication variceal bleeding. But, despite the Baveno VI recommendations on the management of portal hypertension suggesting performing early TIPS in high-risk cirrhotic patients with AVB, only 10% of those eligible undergo the procedure, a key reason being the concern for developing HE.

In the multicentre, observational study, the prevalence of HE on admission and the outcomes of early TIPS in high-risk patients with AVB were assessed, as well as the utility of HE at admission as an independent factor to predict death or HE progression in high-risk cirrhotic patients. Through the investigation of >2,000 patients across 34 centres, the study found that the frequency of HE presence at admission was significantly higher in high- versus low-risk patients with cirrhosis (38.1% versus 10.6%; p=0.008).

Investigation of the survival of patients with HE at admission highlighted an association between early-TIPS placement and significantly improved survival. Furthermore, there were less recurrent HE events compared to those who received endoscopic and drug treatment (hazard ratio: 0.453; 95% confidence interval: 0.218–0.940; p=0.003, 16.7% versus 27.3%; p=0.04, respectively). Dr Marika Rudler, Groupe Hospitalier Pitié-Salpêtrière-Charles, Paris, France, explained: "Although HE at admission is independently associated with poor survival in high-risk patients with AVB, early TIPS significantly improved survival, recovery of HE, and decreased the occurrence of new HE episodes after AVB."

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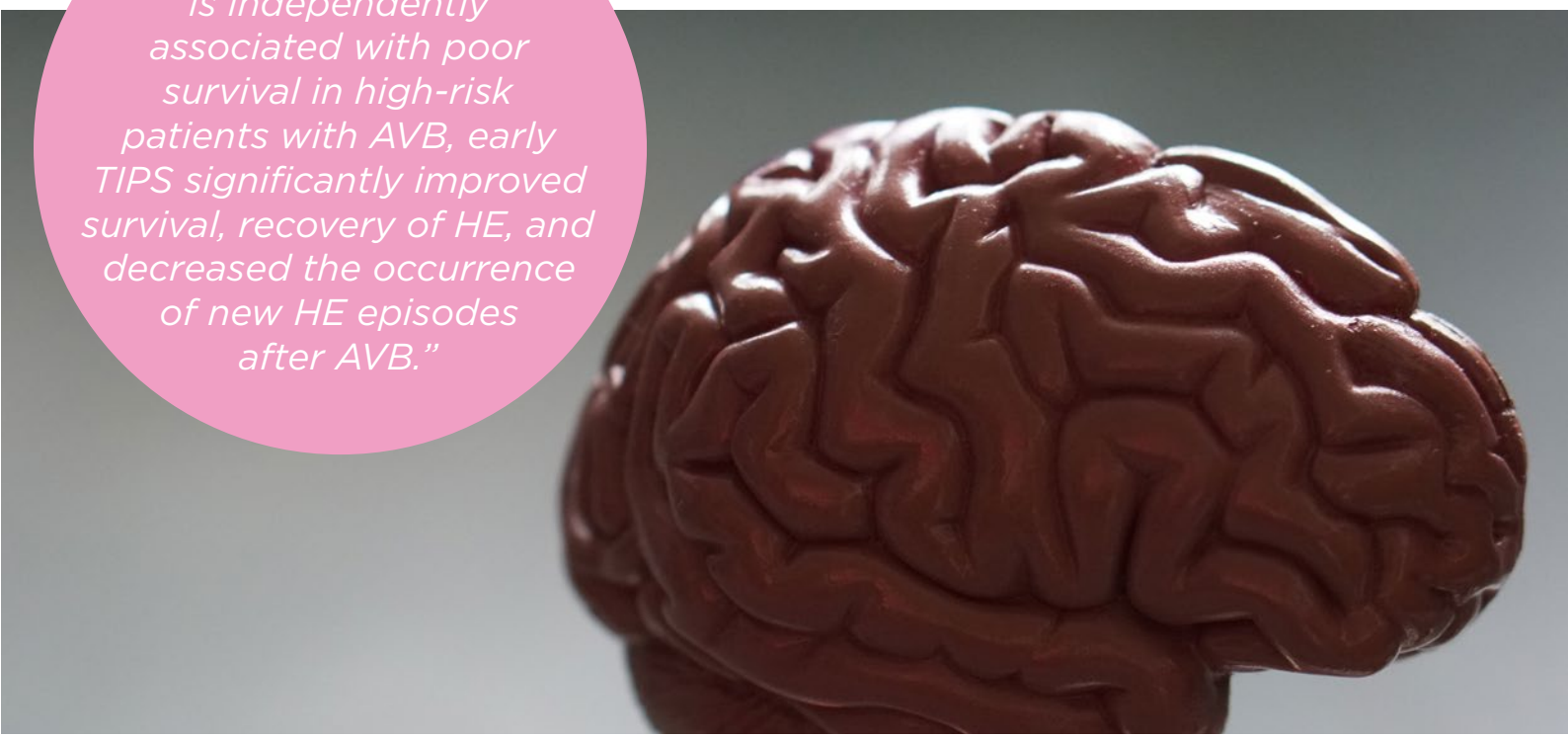

A Wide Field of Novel Treatments for Chronic Hepatitis B

NEW agents have shown promise for a functional cure for chronic hepatitis B virus (HBV) infection. The results of early trials for several novel agents were presented at The Digital ILC 2020 and in a press release dated 28th August 2020, with evidence of early progress in combatting this chronic liver disease discussed.

Current treatments for chronic HBV infection can suppress viral replication, but rarely result in a functional cure, defined by loss of detection of the hepatitis B surface antigen (HBsAg). The two currently approved treatments for chronic HBV infection are nucleos(t)ide reverse transcriptase inhibitors (NRTI) and interferon-α. The new agents discussed at The Digital ILC 2020 exploit different mechanisms to address HBV infection: disruption of viral proteins, including HBsAg; direct inhibition of the HBV core protein; and immune system targeting.

Four studies at The Digital ILC 2020 discussed trial results of agents that target the production of viral proteins, either by RNA interference (RNAi) or using antisense oligonucleotides.

A further study examined the impact of targeting the viral core protein directly in patients who were already virologically suppressed on NRTI therapy; this study found a greater percentage of patients went on to have HBV DNA <5 IU/mL compared to baseline in the treatment group versus placebo (63% at baseline to 94%, versus 80% to 70% with placebo). A final study considered the strategy of improving the innate immune response to chronic HBV infection; there were dose-proportional increases in cytokines, changes in immune cells, and 5% of patients receiving the new agent (a toll-like receptor 8 agonist) had a loss of HBsAg.

"The development of novel therapeutics for persistent HBV infection is currently one of the most vibrant fields in hepatology," outlined Dr Tobias Böttler, University Hospital Freiburg, Germany, and a member of the EASL Governing Board. "With so many different approaches that show promising results regarding HBsAg-decline, and even HBsAg-loss, we appear to be edging closer to the development of a functional cure."

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Patients with Diabetes: A Hidden Population Living with Advanced Liver Disease?

TYPE 2 diabetes mellitus (T2DM) has been uncovered to be highly associated with liver fibrosis, according to a pilot study conducted in two primary care centres in North East England, UK. The results of the study were published in a press release at The Digital ILC 2020, dated 28th August 2020.

Up to 25% of adults worldwide are thought to be affected by nonalcoholic fatty liver disease (NAFLD), the liver manifestation of metabolic syndrome. NAFLD is progressive and leads to fibrosis through accumulation of fat deposits in the liver, which leads to inflammation and scarring. In severe conditions, it progresses to nonalcoholic steatohepatitis (NASH). Despite being a risk factor for NAFLD, patients with T2DM are not universally screened for NASH or fibrosis.

This pilot study assessed 477 successive patients with T2DM between April 2018 and September 2019. If older than 35 years, patients had their fibrosis-4 (FIB-4) score measured; 84 patients had a FIB-4 above their age-specific cut-off. If a patient had a liver stiffness measurement of ≤8 kPa they remained in primary care and were advised to repeat staging in 3 years; however, 24 patients had a measurement of >8 kPa, and therefore were referred to secondary care. If a patient was suspected of having advanced fibrosis, they were enrolled into a surveillance programme.

Overall, results showed that 4.8% of the participants had advanced liver fibrosis, a 7-fold increase compared to the centre's previous T2DM cases. Additionally, >50% of those who received a diagnosis of significant fibrosis or advanced liver disease would not have been diagnosed had national guidelines been followed, as they presented with normal alanine aminotransferase levels.

Prof Emmanuel Tsochatzis, University College London, London, UK, and EASL Governing Board member, emphasised the clinical importance of the study for patients with diabetes and missed NAFLD diagnoses: "We cannot rely on clinical judgment or abnormal liver tests for this and we do need staging pathways with noninvasive fibrosis assessment in primary care or diabetic clinics."

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Novel Models to Predict Hepatocellular Carcinoma

IMPROVED understanding of who is most at risk of developing hepatocellular carcinoma (HCC) following hepatitis C virus infection could have an important impact on how screening programmes are implemented. This may now be easier than expected as two independent research teams have developed new predictive models for HCC in patients who achieved a sustained virological response (SVR) to direct-acting antiviral (DAA) therapy. These results were presented in a press release at The Digital ILC on 27th August 2020.

Although DAA therapy can achieve SVR in >95% of patients with chronic HCV infection, these patients continue to have a residual risk of HCC, particularly those with underlying liver disease or comorbidities. Prediction models and risk factors for HCC in HCV-infected patients prior to eradication is well understood; however, these have not yet been established in patients who achieve SVR with DAA therapy.

A French research team used data from patients with biopsy-proven compensated cirrhosis from the French ANRS CirVir prospective cohort. They aimed to identify characteristics associated with patients likely to develop HCC after HCV eradication according to serum alpha-fetoprotein and routine serum biomarkers. The cohort included 142 out of 717 patients with HCV at baseline and 47 out of 413 who achieved SVR developed HCC, over a median follow-up period of 74.2 months. Results identified that patients with elevated serum parameters (n=95; 13.7% HCC incidence) and with impaired liver function (n=109; 15.6% HCC incidence) had an elevated risk of developing HCC among those who achieved SVR.

In an Egyptian study, 2,326 patients with chronic HCV infection and advanced hepatic fibrosis or liver cirrhosis who achieved an SVR were followed for an average of 24 months. Here, 109 patients (4.7%) developed HCC during the follow-up period. Risk factors included age, sex, serum albumin, alpha-fetoprotein, and pretreatment fibrosis stage. These variables were used to develop a simple scoring system, which stratified patients into low-, medium-, and high-risk groups with a good predictive accuracy. Cumulative incidence of HCC in these groups after 2 years was 2.0%, 4.5%, and 10.3%, respectively. If validated, the simple scoring system could help to individualise HCC screening of HCV-infected patients after successful DAA treatment.

Dr Jordi Bruix, EASL Governing Board member, noted that: "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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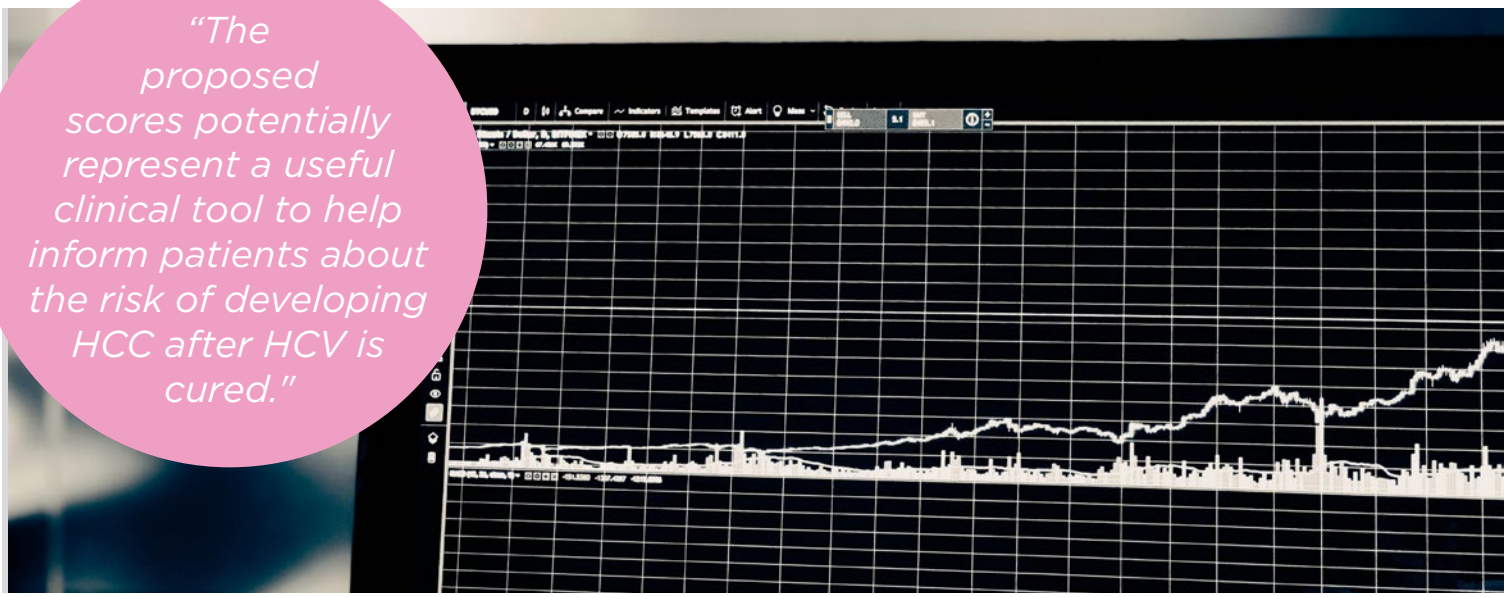

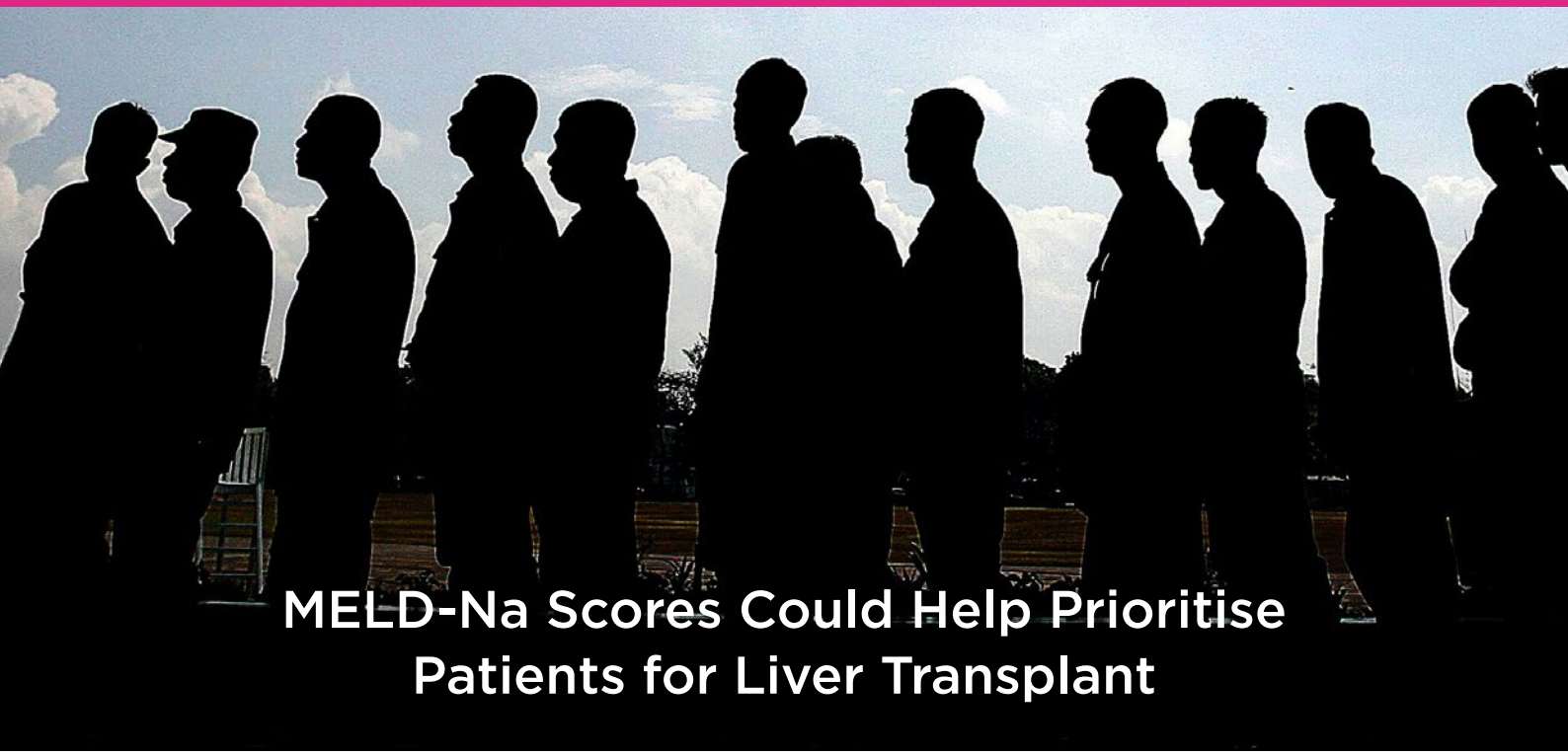

MELD-Na Scores Could Help Prioritise Patients for Liver Transplant

"This study is an important step in introducing MELD-Na in the European liver transplant programmes, as it demonstrated an almost 5% improvement in 90-day waiting list mortality."

THE MODEL for End-stage Liver Disease-Sodium (MELD-Na) score, as opposed to the more commonly used MELD score, may be more optimised for prioritising patients for liver transplantation. This is according to a study, the results of which were announced in a press release dated 27th August 2020 at The Digital ILC 2020, conducted by researchers at Leiden University Medical Center, Leiden, the Netherlands, who used data from the Eurotransplant network.

More than 5,000 patients with chronic liver disease who were placed on the Eurotransplant liver transplant waiting list between 2007 and 2008 were included in the study. The MELD score had been used to determine the priority of each transplant, and the researchers of the study reclassified the patients retrospectively based on their MELD-Na score.

Results showed that 26.3% of patients who had died within 90 days of listing would have had a significantly higher chance of receiving a transplant if they had been classified by MELD-Na. Additionally, 40% of the patients had been diagnosed with hyponatraemia, which was associated with a 3-fold increased risk of mortality within 90 days of being listed.

Dr Ben Goudsmit, who presented the results at The Digital ILC 2020, stated: "We believe that MELD-Na-based allocation would help to prioritise 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."

By identifying the patients most in need of treatment, and with the global shortage of liver grafts and the increasing prevalence of cirrhosis, Dr Goudsmit hopes that using MELD-Na-based allocation will reduce the mortality rate of patients on the transplant list.

Prof Emmanuel Tsochatzis, University College London, London, UK, and EASL Governing Board member, explained that use of the MELD score has been a breakthrough in chronic liver disease treatment, but it is becoming apparent that the addition of Na to the equation is vital for improving classification of patients. He praised the study: "This study is an important step in introducing MELD-Na in the European liver transplant programmes, as it demonstrated an almost 5% improvement in 90-day waiting list mortality."

New Treatments Improve Biomarkers in Fatty Liver Disease

NOVEL pharmacological therapies have shown promise in the treatment of nonalcoholic fatty liver disease (NAFLD). While there are no currently approved therapies for NAFLD, new treatments have demonstrated an ability to improve biomarkers of the disease, as highlighted in a press release from The Digital ILC 2020, dated 27th August 2020.

NAFLD, including nonalcoholic steatohepatitis (NASH), is thought to affect 25% of the world's population. It is the fastest-growing liver disease globally and can increase risk of hepatocellular carcinoma and cirrhosis. An estimated 37.3% of people with Type 2 diabetes mellitus (T2DM) have concurrent NASH; this overlap has led to investigation of lipid metabolism and inflammation pathways as potential treatment avenues.

"These clinical studies show that targeting FXR, GLP-1, and gastrointestinal hormone receptors are promising approaches for the treatment of NASH, which are worth being further evaluated."

The farnesoid X receptor (FXR) negatively regulates hepatic gluconeogenesis, lipogenesis, and steatosis. EDP-305, a novel FXR agonist, was studied in 132 patients with fibrotic NASH without cirrhosis. Those treated with 2.5 mg of EDP-305 saw significant reductions compared to placebo in alanine aminotransferase, fat percentage (measured by MRI-proton density fat fraction), γ-glutamyl transferase, C4 as a pharmacodynamic marker, and high-density lipoprotein. The most common treatment-emergent adverse event was pruritis, leading to discontinuation in 20.8% of patients receiving 2.5 mg and 1.8% of patients receiving 1 mg of EDP-305.

The glucagon-like peptide-1 (GLP-1) receptor decreases appetite, and influences hepatic lipid content and inflammation, to improve glucose control and reduce body weight. A second study explored the impact of the first-in-class GLP-1/glucagon dual-receptor agonist cotadutide on 834 patients with T2DM who were overweight or obese, over a period of 54 weeks of treatment. At the end of treatment, significant reductions in body weight and alanine aminotransferase were noted with cotadutide 300 µg compared to placebo and an open-label once-daily 1.8 mg dose of liraglutide. This was further confirmed by improvements in NAFLD fibrosis score and FIB-4 with cotadutide 300 µg versus placebo.

Representing the EASL Scientific Committee, Prof Luca Valenti, University of Milan, Italy, highlighted the value of these findings: "These clinical studies show that targeting FXR, GLP-1, and gastrointestinal hormone receptors are promising approaches for the treatment of NASH, which are worth being further evaluated."

Addition of Bezafibrate May Improve Primary Biliary Cholangitis Outcomes

"As response to UDCA can now be anticipated from pretreatment features, a new treatment approach may be to start bezafibrate combination therapy immediately in patients with a predicted poor response to UDCA"

BEZAFIBRATE, a hypolipidaemic fibrate, in combination with ursodeoxycholic acid (UDCA) has growing evidence for its use in treating primary biliary cholangitis (PBC). According to a study of a Japanese cohort, which was presented at The Digital ILC 2020 and reported in a press release dated 27th August 2020, this combination therapy improved transplant-free survival for patients with PBC when compared to UDCA monotherapy or no treatment.

Current evidence suggests that biochemical markers and long-term outcomes are both improved by the addition of bezafibrate to UDCA therapy for PBC, an immune-medicated liver disease. Progression of symptoms can lead to cirrhosis and liver failure, putting those with PBC at risk of requiring a liver transplantation. This risk is further increased if patients with PBC do not respond adequately to UDCA, which is the case for approximately 20% of patients, despite UDCA being the recommended first-line treatment for PBC in Europe.

In the large nationwide cohort (N=8,180), patients with PBC either received UDCA monotherapy (6,087; 74.4%), a combination of UDCA and bezafibrate (943; 11.5%), no treatment (1,133; 13.9%), or bezafibrate monotherapy (17; 0.2%). A significant decrease in the risk of all-cause mortality or liver transplantation was observed in those treated with UDCA monotherapy versus those who did not receive any treatment (adjusted hazard ratio: 0.55; 95% confidence interval: 0.47–0.65; $p<0.0001$). Compared to UDCA monotherapy, the combination of bezafibrate and UDCA further reduced this risk (adjusted hazard ratio: 0.23; 95% confidence interval: 0.15–0.35; $p<0.0001$).

"As response to UDCA can now be anticipated from pretreatment features, a new treatment approach may be to start bezafibrate combination therapy immediately in patients with a predicted poor response to UDCA," theorised Dr Atsushi Tanaka, Teikyo University School of Medicine, Tokyo, Japan, presenter of the study's findings. To confirm the long-term effectiveness of the addition of bezafibrate to routine UCDA treatment, Dr Tanaka acknowledged the need for prospective, randomised, placebo-controlled studies.

Treatment Option for Viral Hepatitis High-Dose Bulevirtide

Bulevirtide, a first-in-class entry inhibitor treatment for patients with hepatitis B virus (HBV)/hepatitis D virus (HDV) coinfection, has been proven to be safe and effective in a study focussed on high-dose regimens. This is according to the results of a new study that was presented as part of a press release dated 28th August 2020 at The Digital ILC 2020.

The potential new treatment option was investigated for safety and efficacy in both single-drug therapy and in combination with pegylated interferon α (PEG-IFNα), the only treatment option currently recommended for HDV. Over the 48-week treatment period, declines in HDV RNA were monitored. Patients with chronic HBV/HDV coinfection were randomised to either bulevirtide 10 mg once daily and PEG-IFNα 180 µg once weekly, or bulevirtide 5 mg twice daily with tenofovir disoproxil fumarate. Patients were treated for 48 weeks, followed by a 24-week period of either being treatment-free or having tenofovir disoproxil fumarate only.

The results at the end of the treatment period showed a decrease in serum HDV RNA levels: these were undetectable in 86.7% and 40.0% of the patients in the groups bulevirtide 10 mg once daily and PEG-IFNα 180 µg once weekly, and bulevirtide 5 mg twice daily with tenofovir disoproxil fumarate, respectively. Alanine aminotransferase was also shown to have decreased and 26.7% and 40.0% of patients achieved normalised levels of alanine aminotransferase after 48 weeks, in the groups bulevirtide 10 mg once daily and PEG-IFNα 180 µg once weekly, and bulevirtide 5 mg twice daily with tenofovir disoproxil fumarate, respectively. Notably, HBsAg, indicative of HBV infection, became undetectable in one patient in the treatment arm bulevirtide 10 mg once daily and PEG-IFNα 180 µg once weekly. These results suggested the patient achieved 'functional cure'. The researchers recorded 143 treatment-related nonserious adverse events. The study lead, Prof Heiner Wedemeyer, Hannover Medical School, Hannover, Germany, reflected on the importance of this data, explaining that the "high-dose administration of bulevirtide coadministered with PEG-IFNα or TDF for 48 weeks was safe and well tolerated in patients with HBV/HDV coinfection." He also commented on the prospects of the results: "This trial offers new treatment options for the most severe form of viral hepatitis."