Treatment advances for Non-Alcoholic Fatty Liver Disease (NAFLD) announced at ILC 2021

Breakthrough drug for Europe´s fastest growing disease announced at the International Liver Congress 2021

GENEVA, SWITZERLAND, June 25, 2021 /EINPresswire.com/ -- For Immediate Release

> We are clearly in a race against time to develop new drugs and treatment for NAFLD before the epidemic worsens."
>
> *Philip Newsome*

Media Release

Treatment advances for Non-Alcoholic Fatty Liver Disease (NAFLD) announced at ILC 2021

New data released on trials involving RNAi therapeutics, antivirals and structurally engineered fatty acids to treat NAFLD

Friday 25 June 2021 (Geneva, Switzerland)-- Leading hepatology researchers announced important new developments in the treatment of Non-Alcoholic Fatty Liver Disease (NAFLD) at the International Liver Congress 2021 (ILC 2021) today. This includes new data on trials involving RNAi therapeutics, antivirals and structurally engineered fatty acids to treat NAFLD which is now one of the fastest growing diseases globally.
Linked to growing rates of obesity and diabetes, NAFLD has emerged as the most prominent cause of chronic liver disease worldwide and occurs in about one quarter of the global population. Experts predict that over the next decade, NAFLD will become the leading cause of end stage liver disease and liver transplantation.

Liver disease is on the rise and the fastest growing cause of death in the UK compared to other major killer diseases, such as heart disease and cancer, in which the number of deaths have either remained stable or decreased. In the UK liver disease is the biggest cause of death in those aged between 35-49 years old. NAFLD is already the fastest growing cause of hepatocellular carcinoma (HCC), the commonest form of liver cancer in the USA, France and the UK. Non-alcohol related steatohepatitis (NASH) is the second, more serious stage of NAFLD.

"We are clearly in a race against time to develop new drugs and treatment for NAFLD before the epidemic worsens," said Philip Newsome, General Secretary of EASL and Professor of Experimental Hepatology and Director of the Centre for Liver Research at the University of

Birmingham in the UK.

“News that Resmetiron appears to make inroads against NASH is most welcome – we are hopefully beginning to draw a line in the sand on the treatment of fatty liver disease.”

Today’s official press conference highlighted five studies covering treatment research for NAFLD and NASH selected from over 1500 abstracts being presented at ILC 2021.

Food Insecurity lined to death of Adults with Non-alcoholic Fatty Liver Disease and Advanced Fibrosis

This study followed 34,134 eligible participants followed for a median 7.2 years. 4,816 had NAFLD (mean age 51,58% male, 14% below the poverty line) and 1,654 had advanced fibrosis (mean age 69, 55% male, 15% below the poverty line) with food insecurity present in 28% and 21%, respectively.

All-cause age-adjusted mortality was 12 per 1000 person-years among NAFLD participants (11 if food secure, 15 if food insecure) and 32 per 1000 person-years among advanced fibrosis participants (28 if food secure, 50 if food insecure). In multivariate models adjusted for age, race/ethnicity, poverty-income ratio, education level, insurance status, haemoglobin A1c, body mass index, and smoking, food insecurity was independently associated with higher all-cause mortality among those with NAFLD (HR=1.46, 95%CI:1.08-1.97) and those with advanced fibrosis (HR=1.37; 95%CI:1.01-1.86) (Figure).

Ani Kardashian of the University of Southern California in the U.S. reported that a significant interaction between food insecurity and poverty-income ratio among those with advanced fibrosis (p=0.015. Food insecurity was associated with greater mortality in adults with advanced fibrosis and poverty (HR=2.27, 95%CI:1.41-3.66), but not among those without poverty (HR=1.09, 95%CI:0.66-1.59).

Kardashian concluded that Food insecurity is significantly associated with greater all-cause mortality in adults with NAFLD and advanced fibrosis, independent of other known causes and recommended that interventions that address food insecurity among adults with liver disease should be prioritized to improve health outcomes in this population.

Abstract: Food Insecurity is Associated with All-Cause Mortality in U.S. Adults with Non-alcoholic Fatty Liver Disease and Advanced Fibrosis (GS-1072)

Session: General Session, Thursday 16:00-17.30

ARO-HSD reduces hepatic HSD17B13 MRNA expression and protein levels in patients with suspected NASH (LBP-2580)

HSD17B13 is a member of the hydroxysteroid dehydrogenase family involved in the metabolism of hormones, fatty acids, and bile acids. Human genetic data indicate that a loss-of-function mutation in HSD17B13 provides strong protection against alcoholic and non-alcoholic steatohepatitis. ARO-HSD
is an investigational GalNAc-conjugated RNAi therapeutic designed to replicate this observed protective loss-of-function effect by knocking down HSD17B13 expression in hepatocytes. This study reports initial results from the ongoing first in human clinical study, AROHSD1001 (NCT04202354), in healthy volunteers (HVs) and patients with NASH or suspected NASH.

ARO-HSD was administered by subcutaneous injection to male and female HVs (19-52 yrs old) in a single-dose escalation design at doses of 25, 50, 100 and 200 mg (4 active, 4 placebo per dose level) and followed to Day 113. Five patients (40-50 yrs old) with suspected NASH (based on MRI-PDFF
liver fat >8% and ALT>ULN) administered 100 mg ARO-HSD have completed the Day 71 biopsy. Safety was assessed in all subjects including laboratory measures of liver function. A liver biopsy was collected at baseline and Day 71 in patients and change from baseline in hepatic HSD17B13 mRNA expression and protein levels were measured. Additional multi-dose patient cohorts will be analysed following availability of the Day 71 liver biopsies.

Rohit Loomba of the University of California in the U.S noted that ARO-HSD was well-tolerated in both HVs and patients with no ARO-HSD related serious adverse events reported, no AE-related drug discontinuations, and no ARO-HSD associated Grade 3 or 4 laboratory abnormalities (NCI-CTCAE v5.0). In all five patients, hepatic HSD17B13 mRNA decreased by a mean of 84% (range: 62-96%) from baseline. Two patients had a protein decrease of 92% and 97%, while the other 3 patients Day 71 measurements were below the assay's level of quantitation. Patients had a mean decrease from baseline in ALT of 46% (26-53%) at Day 85. There were no significant changes in weight or lipid parameters.

Gane concluded that ARO-HSD is the first investigational RNAi therapeutic to demonstrate robust inhibition of HSD17B13 mRNA and protein expression with associated reductions in AL and recommended the continued development of ARO-HSD in patients with alcoholic and non-alcoholic steatohepatitis.

Abstract: ARO-HSD reduces hepatic HSD17B13 MRNA expression and protein levels in patients with suspected NASH (LBP-2580)

Icosabutate, an engineered fatty acid, significantly reduces relevant markers of NASH and fibrosis in 4 months

Icosabutate (ICO) is a novel, oral, once-daily, liver-targeted, engineered eicosapentaenoic acid derivative with potent anti-inflammatory and antifibrotic effects acting primarily through the G-coupled protein receptor (GPR120) and the arachidonic acid signalling pathways related signalling pathways. The ICONA trial is an ongoing 52-week, multicentre, placebo-controlled,

phase 2b study enrolling 264 subjects with biopsy confirmed NASH.

Rapid, sustained, and significant dose-dependent decreases were seen with both doses in ALT, AST, GGT, and ALP at levels predictive of histologic improvement. The 600 mg dose showed significant reductions in PRO-C3 and ELF score (both total score and individual components) supporting an effect on fibrogenesis. hsCRP significantly decreased by 52% with 600 mg in conjunction with improvements in glycemic control and key atherogenic lipoproteins. There was no change in weight or BMI suggesting a treatment effect independent of weight loss. Both LFC and cT1 were unchanged which is consistent with ICO mechanism of action. Treatment was well tolerated with no evidence of hepatoxicity, cardiovascular events or other safety concerns as confirmed by an independent DSMB.

Arun Sanyal of the Virginia Commonwealth University, Richmond in the U.S. noted that treatment of NASH patients with ICO for 16 weeks had a dose-dependent improvement in multiple relevant biologic pathways, with broad and potent effects on markers of liver injury, inflammation and fibrogenesis along with improvements in glycemic control and atherogenic lipids. Sanyal concluded that these data, combined with a favourable safety profile to date, support a potential for impacting liver histology at 52 weeks as well as improving common comorbid conditions seen in NASH patients.

Abstract: Icosabutate, a novel structurally engineered fatty acid, significantly reduces relevant markers of NASH and fibrosis in 16 weeks: interim analysis results of the ICONA trial (LBP-2907)

Resmetirom reduces fibrosis in Phase III NASH trial

This study reported results from a 52- week Phase III registrational double blind placebo-controlled NASH clinical trials to study the effect of Resmetirom in more than 2000 NASH patients.

169 patients were enrolled in the open label arm, all completed 16 weeks, and 64 had completed 52 weeks. Demographics include mean age 55.7 (11.5 (SD)), female 69%, BMI 35.8 (6.0), diabetes 43%, hypertension 62%, dyslipidaemia >70%, mean ASCVD score 11.5%. Fibroscan (kPa 7.7 (3.6)), and mean MRI-PDFF 18% (7%) are consistent with F2 stage NASH. Statistically significant ($p<0.0001$) MRI-PDFF reduction of 53% (3.3% (SE)) fat fraction overall, and 62% reduction in a SHBG responder group were observed at Week 52. MRE was statistically significantly reduced at Weeks 16 and 52 (Table). At week 52 Fibroscan CAP and kpa were reduced relative to baseline. LDL-C (-23% (2.3% (SE))), apolipoprotein-B (-22% (2.3%)), triglycerides (med, -32(7.8) mg/dL), and lipoprotein(a) (-39% (4.6%)) were statistically significantly reduced compared to baseline. Decreases from baseline: ALT -22 IU, AST -12 IU, GGT -25 IU($P<0.0001$). Statistically significant reductions in inflammatory and fibrosis biomarkers hsCRP, reverse T3, ELF and M30 were observed. No safety flags were identified.

Stephen Harrison, Visiting Professor of Hepatology at the University of Oxford in the UK reported

that noninvasively identified NASH patients treated with 100 mg per day of Resmetirom for up to 52 weeks demonstrated rapid and sustained reduction in 1-hepatic fat; 2-fibrosis stage as assessed by biomarkers, MRE and fibroscan; 3- LDL and atherogenic lipids, 4-liver enzymes and inflammatory biomarkers. Harrison concluded that the results supported the use of non-invasive tests to monitor individual NASH patient response to Resmetirom treatment.

Abstract: Reduction in fibrosis and steatohepatitis imaging and biomarkers in a Phase III 52-week Resmetirom NASH trial (GS-2563)
Session: Friday June 25, 16:00-17:30

Development and validation of Agile 3+: novel Fibroscan based score for the diagnosis of advanced fibrosis in patients with non-alcoholic fatty liver disease (OA-555)

Currently available non-invasive tests, including FIB-4 and liver stiffness measurement (LSM) by Vibration Controlled Transient Elastography (VCTE), are highly effective in excluding advanced fibrosis (F >= 3) yet their ability to rule it in is moderate. This study aimed to develop and validate a new score (Agile 3+), to identify advanced fibrosis in NAFLD patients,
This multi-national, retrospective study included seven cohorts of adults with suspected NAFLD who underwent liver biopsy (LB), LSM by VCTE, and blood sampling in either routine clinical practice or during screening for clinical trials.

Jerome Boursier of Angers University Hospital in France note that in all datasets - platelets, gender, age and presence of diabetes mellitus Agile 3+ outperformed LSM and FIB-4.
Abstract: Development and validation of Agile 3+: novel FibroScan based score for the diagnosis of advanced fibrosis in patients with non-alcoholic fatty liver disease (OA-555)
Session: Saturday June 26, 10:00-11:30
Further information:

Media Registration: Accredited media can apply for free registration here.
Press Programme: The Official Press Programme can be found here.
All ILC 2021 Official Press Conferences will broadcast be live on Zoom for registered media.
Embargo Policy: Please note that the ILC2021 Embargo Policy has changed this edition -media representatives are asked to familiarise themselves with the new policy.

--END--

Further Information:
Michael Kessler
Michael Kessler Media
EASL Media Relations
Email: michael.kessler@intoon-media.com
Mob: +34 655 792 699
Twitter: @mickessler

About The International Liver Congress™
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.

About The European Association for the Study of the Liver (EASL)
Since its foundation in 1966, this not-for-profit organisation has grown to over 4,500 members from all over the world, including many of the leading hepatologists in Europe and beyond. EASL is the leading liver association in Europe, having evolved into a major European association with international influence, and with an impressive track record in promoting research in liver disease, supporting wider education, and promoting changes in European liver policy.

Michael Kessler
Michael Kessler Media - EASL Media relations
+34 655 79 26 99
email us here
