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## Abstracts of the 2022 Annual Meeting of the ALEH (Asociación Latinoamericana para el Estudio del Hígado)

### P1- HIGH VIRAL SUPPRESSION AND IMPROVED SAFETY PROFILE OF TENOFOVIR ALAFENAMIDE RELATIVE TO TENOFOVIR DISOPROXIL FUMARATE IN CHRONIC HEPATITIS B PATIENTS TREATED FOR 5 YEARS

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**Introduction and Objectives:** Tenofovir Alafenamide (TAF) is a preferred treatment in the most recent EASL and AASLD HBV Guidelines, especially in patients with risk factors for TDF-associated renal and bone effects. In 2 identically-designed double-blind (DB), randomized (2:1), Phase 3 studies (HBeAg-negative

patients [N=425] and HBeAg-positive patients [N=873]), TAF demonstrated antiviral efficacy non-inferior to that of TDF with superior renal and bone safety. After completing three years of DB treatment, all patients were eligible to receive open-label (OL) TAF through Year eight. Here we present study results for Year five.

**Materials and Methods:** Efficacy was assessed by serial virologic, biochemical, and serologic assessments, while safety data included changes in renal function and changes in hip and spine bone mineral density. Resistance testing and phenotyping were performed annually through Year 5.

**Results:** Of 1298 randomized and treated patients, 1157 (89%; 775 TAF; 382 TDF) entered OL, at year 5, 999 (77%; 675 TAF, 136 TDF/TAF OL 3y, 188 TDF-TAF OL 2y) patients remained on treatment. High rates of virologic control were achieved and maintained in patients receiving TAF throughout and for TDF patients who switched to TAF at Weeks 96 or 144. Rates of ALT normalization and serologic responses were also comparable among groups. Eight patients are undergoing phenotypic testing to assess resistance. Adverse events (AEs) leading to discontinuation were low and similar among groups. Renal and bone outcomes were improved following the switch to OL TAF from TDF.

**Conclusions:** After five years of treatment, virologic suppression rates remained high, and TAF was safe and well tolerated, with improved renal and bone safety in patients switching from TDF.

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### P-2 DE NOVO LIPOGENESIS MARKERS ARE INVOLVED IN METABOLIC ASSOCIATED FATTY LIVER DISEASE PROGRESSION IN BTBR OB/OB MICE

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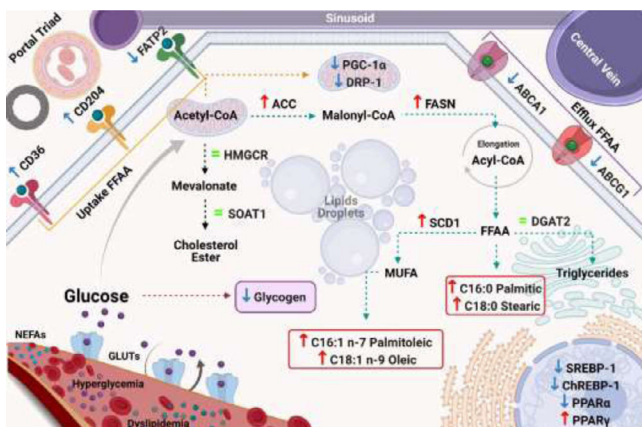
**Introduction and Objectives:** The new recommendations suggesting changing the current nomenclature from Non-Alcoholic Fatty Liver Disease (NAFLD) to Metabolic associated fatty liver disease (MAFLD) are primarily aimed at improving the understanding of the disease. MAFLD is a hepatic manifestation of metabolic syndrome and is usually associated with obesity and type 2 diabetes, excluding other causes not associated with positive energy balance. This study aimed to characterize the pathophysiological mechanism involved in MAFLD development in susceptible-strain Black Tan and brachyuric (BTBR) insulin-resistant mice in combination with leptin deficiency (ob/ob).

**Materials and Methods:** We studied liver morphology and biochemistry on our diabetic and obese mice model (BTBR ob/ob) as well as a diabetic non-obese control (BTBR + streptozotocin) and non-diabetic control mice (BTBR wild type) from 4–22 weeks. The lipid composition was assessed and lipid-related pathways were studied at transcriptional and protein levels.

**Results:** Microvesicular steatosis was evident in BTBR ob/ob from week 6, progressing to macrovesicular in the following weeks. At the 12th week, inflammatory clusters, activation of STAT3 and Nrf2 signaling pathways, and hepatocellular ballooning. At 22 weeks, the histopathological features previously observed were maintained and no signs of fibrosis were detected. Liver gene-expression analysis demonstrated modifications in fatty acid transporters associated with uptake (Cd36, Cd204, Fatp4)/efflux (Abca1, Abcg1), *de novo* fatty acid synthesis enzymes (ACC, FASN, SCD-1) and transcription factors related to lipogenic pathways (Pparα/γ, Srebp-1, Chrebp-1). Additionally, the lipidomic analysis showed profiles associated with *de novo* lipogenesis (DNL), showing a significant increase in palmitic acid (C16:0), palmitoleic acid (C16:1n7) and oleic acid (C18:1n9).

**Conclusions:** BTBR ob/ob mice develop MAFLD profiles that resemble pathological features observed in humans, with overactivation of inflammatory response, oxidative stress and DNL signaling pathways. Therefore, BTBR ob/ob mouse is an excellent model for the study of the steatosis to steatohepatitis transition.

**Figure 1:**



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### P-3 PLASMA EXCHANGE WITH ALBUMIN INCREASES EFFECTIVE ALBUMIN LEVELS IN PATIENTS WITH ACUTE-ON-CHRONIC LIVER FAILURE

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**Introduction and Objectives:** Non-oncotic albumin functions such as transport, antioxidant and immunomodulatory capacities may be associated with the beneficial effects of albumin therapy in liver disease patients. For acute-on-chronic liver failure (ACLF) patients, characterized mainly by severe systemic inflammation and organ failure, plasma exchange with human serum albumin (PE-A5%) may be an effective treatment. In fact, the effects of PE-A5% on short-term survival in patients with ACLF are currently under investigation (APACHE phase 3 trial, NCT03702920). To characterize albumin levels with intact structure (effective albumin) in patients with ACLF compared with healthy controls (HC) and to assess the effect of PE-A5% treatment on eAlb levels in patients with ACLF.

**Materials and Methods:** Plasma samples from 10 patients included in the Pilot-APACHE trial (NCT01201720) were assessed. This was a prospective, open-label, non-controlled study in which ACLF patients were treated with six PE-A5% for 10 days. At baseline, results were compared with HC (n=10). Albumin post-translational modifications (PTMs) were determined by mass spectrometry (LC\_E-SI\_qTOF-MS). Native albumin (%) (the primary structure preserved form without PTMs) and effective albumin levels (mg/mL) (calculated as (total albumin x native albumin)/100) were evaluated. Results were expressed as median (IQR).

**Results:** At baseline, ACLF patients showed a significantly lower proportion of native albumin, 19.4% (10.0–28.5), compared with HC, 51.3% (49.0–52.6),  $P < 0.0001$ . Similarly, effective albumin levels, 6.8 mg/mL (3.5–8.9), were lower than HC, 19.8 mg/mL (18.9–20.7),  $P < 0.0001$ . This reduction in native albumin was associated with higher cysteinylated and glycosylated isoforms. After six PE-A5%, native albumin (27.6% (17.1–35.3),  $p = 0.036$ ) and effective albumin (10.4 mg/mL (6.4–13.8);  $p = 0.0067$ ) were significantly increased. Remarkably, this effect was observed right after each PE-A5% session.

**Conclusions:** ACLF patients presented albumin structural abnormalities that led to decreased effective albumin levels. PE-A5% not only improved non-oncotic albumin functions<sup>1</sup> but increased structurally preserved albumin in these patients.

<sup>1</sup> J Hepatol 2018;68(Suppl1):S105–S364

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### P-4 RISK OF HCC IN SOUTH AMERICANS ASSOCIATED WITH TLL1 VARIANT SINGLE NUCLEOTIDE POLYMORPHISM

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