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Introduction and Objectives: Previously published regional real-world results of overall survival (OS) in Barcelona Clinic Liver Cancer (BCLC) B and C patients demanded a prospective cohort study nested in a systematic and continuous medical educational networking group. This study aimed to describe and evaluate the treatment decisions in patients with hepatocellular carcinoma (HCC) within BCLC B and C stages.

Materials and Methods: A multicenter prospective cohort study, conducted in different Latin American centers from Argentina, Brazil and Colombia, started on 15th May 2018 (delayed recruitment during COVID locked-down period). Patients within BCLC B or C stages were included. Survival, tumor progression and patterns of treatment suspension were evaluated.

Results: At this second interim analysis (projected final analysis March 2023), 390 HCC BCLC-B or C patients were included (n=15 excluded); mean age 65 years, 75.6% males and 89.5% cirrhotic. Median OS since HCC diagnosis was 27.2 months. Among BCLC-B patients, the most frequent therapy was transarterial chemoembolization (TACE, 42.3%); 51.8% using drug-eluting beads and 47.4% conventional TACE; with a median OS since 1st TACE of 41.9 months. Similar radiological responses after 1st TACE were observed between both modalities. Overall, 48.2% of the cohort received systemic therapy for HCC (n=188), 23.7% still on BCLC-B stage. The most frequent systemic treatments were Sorafenib (74.5%), atezolizumab bevacizumab (17.5%), and lenvatinib (12.2%), with a median OS since systemic therapy of 15.7 months. Lenvatinib or atezolizumab bevacizumab was used as the second line following sorafenib in 5 and 3 patients, respectively. The most common causes of systemic treatment discontinuation were tumor progression and liver function deterioration (15% to 36.4%). Patterns of tumor progression were not specifically associated with prognosis or treatment discontinuation.

Conclusions: Liver function deterioration occurs in a third of patients following systemic therapies. The complexity of treatment decisions underly the need for a multidisciplinary team and the role of hepatologists.

https://doi.org/10.1016/j.aohep.2023.100914

P- 11 PROTUMORIGENIC GALECTINS 1 AND 3 ARE UPREGULATED IN THE LIVER OF MICE EXPOSED TO CONTINUOUS GROWTH HORMONE LEVELS

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Introduction and Objectives: Human and animal evidence revealed a link between growth hormone (GH) and cancer risk. GH excess is implicated in rodent hepatocarcinogenesis. Transgenic mice overexpressing GH (GH-Tg) develop hepatocellular tumors at old ages, with preneoplastic liver pathology similar to that observed in humans at a high risk of developing hepatic cancer. Galectin 1 (GAL1) is involved in liver tumorigenesis in humans. We reported that GAL1 is upregulated in GH-Tg mice liver, even before histopathological alterations are detected, and particularly enhanced in liver tumors. This study aimed to evaluate if GH modulates the hepatic expression of GAL3, another protumorigenic galectin. As many proteins exhibit sexually dimorphic liver expression, mainly determined by distinct GH secretion patterns between males (intermittent) and females (more continuous), we assessed if GAL1 and GAL3 liver expression was affected by GH secretion patterns.

Materials and Methods: Hepatic GAL1 or GAL3 were analyzed by immunoblotting in GH-Tg mice exposed to continuously elevated GH levels and in Swiss-Webster mice treated with GH during five weeks by implantation of osmotic pumps (continuous treatment) or by two daily injections (intermittent treatment). Statistics: Student's t-test or two-way ANOVA; $P<0.05$, significant; at least nine animals/experimental group.

Results: In GH-Tg mice (both sexes), GAL3 was not increased in the liver at early ages, when minimal histopathological alterations are found, but it was upregulated in young adults with preneoplastic livers and in older mice that develop liver tumors. However, GAL3 was not increased in tumors compared with the adjacent non-tumoral region. In Swiss-Webster mice, GAL1 and GAL3 expression were higher in females than in males. GH continuous treatment produced a significant increase in GAL1 and GAL3 expression in both sexes and loss of sexual dimorphism, while GH injections showed no effect.

Conclusions: GH continuous exposure upregulates protumorigenic GAL1 and GAL3 in mice liver. More studies are required to evaluate its impact on humans.

https://doi.org/10.1016/j.aohep.2023.100915

P- 12 PATHOGENIC VARIANT OF PNPLA3 DOES NOT ASSOCIATE WITH HEPATOCELLULAR CARCINOMA IN SOUTH AMERICANS. A REPORT FROM THE ESCALON NETWORK

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Introduction and Objectives: Hepatocellular carcinoma (HCC) has a strong genetic component and single nucleotide polymorphisms (SNPs) have been consistently associated with HCC risk. Genetic variants in *PNPLA3* have been shown to be frequent in South American populations related to non-alcoholic fatty liver disease (NAFLD). In Caucasian populations, the variant has been shown to increase the risk for HCC when included in Genetic Risk Scores (GRS). Whether this risk applies to other Latino or other populations is unclear.

Materials and Methods: We analyzed blood samples of 217 HCC cases, 120 from South American patients (Argentina, Ecuador, Colombia, Chile and Peru) and 97 from Europeans (Netherlands), as well as 326 cirrhotic controls through the ESCALON network. Genotyping for *PNPLA3* was performed using TaqMan-genotyping assay. Associations between HCC and each SNP were evaluated using logistic regression models.

Results: The median age for HCC in South Americans was 68 y/o (IQR 62-72) and in Europeans, 69 y/o (IQR 60-74), with 59% and 69% of males, respectively. The etiology of liver disease was similar in both groups except for NAFLD/NASH, which accounted for 59% of Hispanics with HCC vs. 25% of Europeans. Proportions of the risk allele of *PNPLA3* were more prevalent among Hispanics (90%) than Europeans (57%). *PNPLA3* G/G was present in 22% of Europeans with HCC compared to 57% of Hispanics. The presence of 2 risk alleles for PNPLA3 was not associated with a higher risk of HCC in South Americans, OR 1.19 (CI 0.58-2.46) or Europeans OR 1.1o (CI 0.34-3.58). When PNPLA3 was added in a GRS with *TM6SF2* and *HSD17B13,* calculating different allele combinations did not associate either with HCC in South Americans,

Conclusions: Our results show that the prevalence of risk alleles in *PNPLA3* differs between South Americans and Europeans. An SNP in *PNPLA3* does not seem to confer an increased risk for HCC in South Americans.

https://doi.org/10.1016/j.aohep.2023.100916

P-13 PREVALENCE, CHARACTERIZATION, AND SURVIVAL OF ACUTE ON CHRONIC LIVER FAILURE IN A LATIN AMERICAN COHORT: A MULTICENTER STUDY

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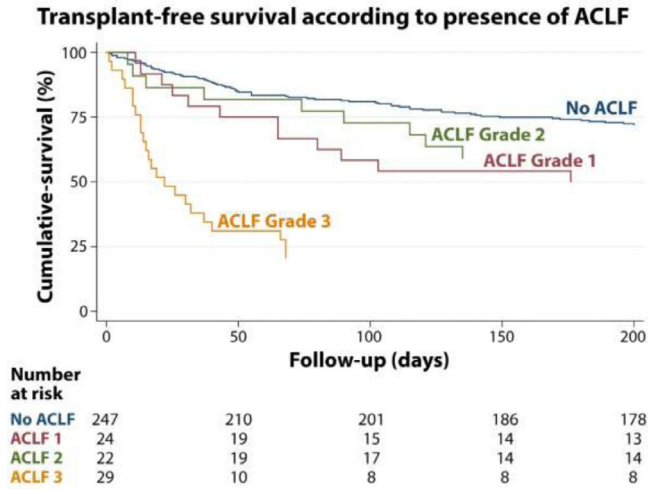
Introduction and Objectives: Acute-on-chronic liver failure (ACLF) is a severe clinical entity with organ failures and high short-term mortality. To Date, few ACLF reports have been published in Latin America. This study aimed to characterize patients with ACLF, identifying triggers, organ failure, and survival at 30, 90, and 180 days compared to patients with decompensated cirrhosis without ACLF.

Materials and Methods: Retrospective study of decompensated cirrhotic patients hospitalized (between 2017-2019) in three centers in Chile. We evaluated transplant-free survival using Kaplan-Meier curves and Cox-regression.

Results: 398 patients were included, a median age of 65.3±11.7-year-old, 50.5% female, 91 (22.9%) presented ACLF (8% ACLF-1, 6.3% ACLF-2, 8.6% ACLF-3); 6.6% underwent liver transplantation. ACLF patients were younger (63.6 vs. 66.0 years; p=0.045), had higher MELD-Na scores (27 [23-32] vs. 17 [13-23]; p<0.001) and higher APACHE II scores (20.5 [16-25] vs. 14 [10-15]; p<0.001) at admission. The most common triggers in both groups were infections (42.4%), gastrointestinal bleeding (23.2%), and alcohol intake (31.3%). Among decompensating factors, acute kidney injury at admission was associated with higher mortality (HR 2.2, 95%CI: 1.4-3.4; p<0.001). The main organ failures were kidney (60.4%), circulatory (49.5%), and brain (48.4%). Organ failures were more frequent in ACLF-3, except renal failure (greater in ACLF-1). Transplant-free survival at 180 days was 73.7% in patients without ACLF and 40% in ACLF (p<0.001). In a Cox regression adjusted by age and sex, transplant-free survival was significantly lower in ACLF-3 compared to patients without ACLF (HR 3.7, 95%CI: 2.3-5.7;p<0.001).

Conclusions: ACLF is an entity of younger patients, with lower global and transplantation-free survival at 180 days and multiple organ failure compared to decompensated cirrhotics without ACLF.



https://doi.org/10.1016/j.aohep.2023.100917