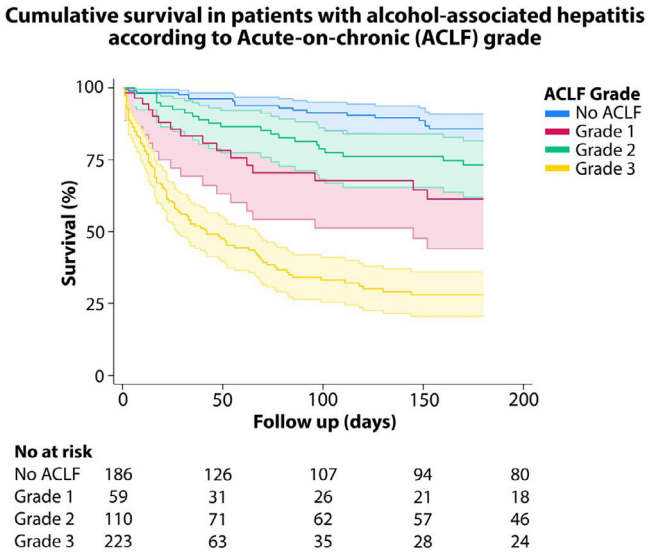
grade 3 should promptly be referred for early LT. The redefinition of ACLF in AH is essential for better quantifying the severity and determining therapeutic goals.



Figure

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OP-6 EVALUATION OF THE HEPATOPROTECTIVE ACTIVITY OF Flourensia cernua AND ITS IMPACT ON THE AEROBIC INTESTINAL MICROBIOTA IN A VALPROIC ACID-INDUCED DAMAGE MODEL IN WISTAR RATS

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Conflict of interest: No

Introduction and Objectives: Liver disease is a health problem that accounts for more than 2 million deaths per year worldwide. Valproic acid (VPA) has been used as a hepatotoxic agent in animal models to reproduce liver damage and test future therapeutic strategies. *Flourensia cernua* (Fc) is a plant that contains compounds with antioxidant activity, which may have a potential hepatoprotective effect.

The aim was to evaluate the hepatoprotective activity of *Flourensia cernua* and its impact on aerobic intestinal microbiota in a valproic acid-induced damage model in Wistar rats.

Patients / Materials and Methods: Seven groups were used (n=6): 1) Sham, 2) VPA, 500 mg/kg of VPA/d/7d i.p., 3) Fc extract at 200 mg/kg/d/3d p.o., 4) Fc extract at 400 mg/kg/d/3d p.o., 5) VPA + Fc 200 mg/kg/d/3d p.o., 6) VPA + Fc 400 mg/kg/d/3d p.o., 7) VPA + Silibinin 200 mg/kg/d/3d p.o.; subsequently, the animals were sacrificed, and samples of faeces, blood, and liver tissue were taken for aerobic intestinal microbiota(AIM), biochemical markers, oxidative stress, and histological analysis, respectively. Data was analyzed using Prism software (v. 10.0.0; GraphPad). $P<0.05$ was statistically significant.

Results and Discussion: VPA significantly increased ALT, AST and decreased total proteins vs. Sham. There was no alteration of transaminases at both tested doses of Fc extract. Only the VPA + Fc 400 mg/kg group showed a significant reduction in ALT, AST, SOD, and MDA vs. VPA, similar to silibinin. The histological analysis did not show significant changes in the study groups. MALDI-TOF primarily identified *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Ochrobactrum intermedium* as AIM in the different study groups.

Conclusions: The hydroalcoholic extract of *F. cernua* did not show toxicity at the evaluated doses, showed a hepatoprotective effect at 400 mg/kg, and did not modify AIM. VPA decreased AIM, and *F. cernua* showed a trend to partially restore the normal bacterial count, similar to silibinin.

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OP-7 Further exploration of differences between lean and non-lean metabolic dysfunction-associated steatotic liver disease (MASLD) in Latino subjects: PNPLA3 frequency and lipidomic profiles

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Conflict of interest: Yes, Fondecyt # 1241450

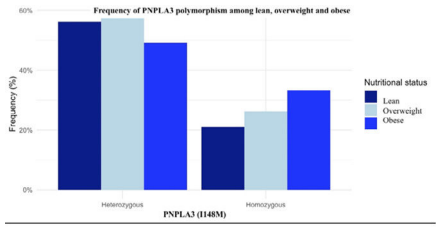
Introduction and Objectives: *Background:* There is limited information on features of lean MASLD patients in Latino subjects. We aimed to analyze the features of MASLD in Chilean patients with normal body mass index (BMI), the frequency of the rs738409 risk polymorphism (PNPLA3 I148M variant) and metabolomic profiles in Chilean individuals with MASLD.

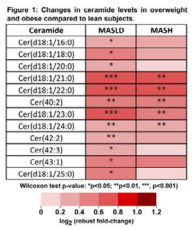
Patients / Materials and Methods: A cross-sectional study involving 181 randomly-selected participants diagnosed with MASLD from the prospective Maule Cohort (BMC Public Health. 2016;16:122). Participants were categorized into lean, overweight, and obese groups

based on their BMI. The presence of the rs738409 polymorphism was examined using Sanger sequencing. Metabolomics was assessed using UHPLC-MS in a separate group of biopsy-proven MASLD patients. Statistical analyses of clinical data and genotypes encompassed Fisher's exact test, Chi-square test, Kruskal-Wallis test.

Results and Discussion: 31.49% (57) were classified as thin, 36.3% (61) as overweight and 39.8% (67) as obese. Higher ALT levels (p=0.004) and body fat percentage in obese subjects were the only significant differences found among the groups. The allelic frequency of rs738409 was similar among groups 77.1%, 83.6% and 82.5% in lean, overweight, and obese subjects, respectively (n.s.). Circulating metabolome showed increased levels of ceramides in overweight and obese patients compared to lean subjects (p<0.001 for five different species). The increment is higher if all the MASLD patients were considered (Figure). Serum bile acids, particularly chenodeoxycholic acid (p<0.001) and glycochenodeoxycholic acid (p=0.024), were also increased. Lipidomic analysis also showed an increase of polyunsaturated diglyceride and triglyceride species in overweight and obese compared to lean subjects. Among them, most of the species included linoleic acid or alpha-linoleic acid in their esterified chains.

Conclusions: PNPLA3 risk allele was equally frequent in lean and non-lean Chilean MASLD patients. Metabolomic differences were found with non-lean subjects exhibiting higher levels of ceramides and bile acid species compared with lean patients. (Supported by Fondecyt # 1241450)





Frequency: percentage of individuals per category.
Heterozygous: CG mutation for PNPLA3 (rs738409).
Homozygous: CC or GG mutation PNPLA3 (rs738409).

PNPLA3 I148M frequency and metabolomic profiles in Chilean patients with MASLD

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OP-8 SECOND LINE THERAPY IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS AND INADECUATE RESPONSE: ARE WE CHOOSING THE RIGHT TARGET POPULATION FOR CLINICALS TRIALS?

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Conflict of interest: No

Introduction and Objectives: Identification of primary biliary cholangitis (PBC) patients who could benefit from second line therapy is uncertain. Most trials rely on 12 month UDCA response assessed by POISE criteria.

Evaluate eligible patients and identify epidemiological-clinical and histological findings that may adversely influence response.

Patients / Materials and Methods: Among 614 patients with established diagnosis of PBC (Jan/16 and Dec/23) 279 were unable to normalize alkaline phosphatase (ALP) and BT after 12 months of UDCA. 107/279 (38.3 %) fulfilled elegibility criteria for second line trials (ALP >1.67, bilirubin <2 and non significant portal hypertension) were analyzed. Fibrosis, bile duct loss, cholangitic and hepatitis activity were obtained in 92/107 patients (Scheuer and Nakanuma scores). All samples were stained with cytokeratin 7. Elastography was done in all patients.

Results and Discussion: Characteristics of patients who fulfilled POISE criteria are described in Table 1. Mean MELD was higher in cirrhotic (9.0vs7.1, p<.001) and correlated with liver events (9.6vs7.0, p<.001). 43/92 patients had moderate-severe ductopenia in histological samples, and it was significantly more frequent in <45 years (66%vs32%, p.008). Moderate-severe portal inflammation with interface hepatitis and lobular spilling was observed in 52/92 samples (56.5%), irrespective of age and correlated with fibrosis. ALP was significantly higher in patients with ductopenia (437.9±207.8vs319.2±162.0, p.01). Elastography correlated with cirrhosis and liver events (10.4vs22.9, p<0.001) but not with inflammation or ductopenia.

Conclusions: A significant proportion of patients unresponsive to UDCA were not eligible for second line trials. Poise criteria eligibility was associated with the presence of ductopenia and advanced fibrosis, particularly in young patients. The presence of moderate to severe portal inflammation is suggestive of ongoing disease activity. Elastography and MELD score correlate with cirrhosis and development of liver events. These findings suggest that we are selecting for second line trials a significant proportion of patients with adverse findings for response. Adverse histological findings might suggest early second line intervention.

Baseline characteristics	Patients (n=92)
Age, mean (years)	55.9 (± 11.8)
Female, num (%)	93 (22.4)
< 45 years, num (%)	22 (22.4%)
Associated autoimmune disease, num (%)	16 (17.3)
Pruritus, num (%)	51 (55.1)
ALP, mean (UI/L)	366.7 (± 192.5)
GGT, mean (UI/L)	366.6 (± 326.2)
ALT, mean (UI/L)	64.7 (± 43.6)
TB, mean (mg/dL)	1.7 (± 4.6)
Elastography >9.6 kPa, num (%)	42 (50%)
MELD score, mean	7.4 (± 1.8)
Cirrhotic, num (%)	17 (16)
Moderate to severe portal inflammation with interface hepatitis and lobular spilling, num (%)	52 (56.5)
AMA, num (%)	80 (86)
Sp100, num (%)	9 (9.7)
GP210, num (%)	8 (8.6)
Under UDCA treatment, num (%)	89 (96.7)

Abbreviations: ALP: alkaline phosfatase, gGT: gamma-glutamyltransferase, ALT: alanine-transferase, TB: total bilirrubine, AMA: antimitochondrial antibody, UDCA ursodeoxycholic acid.

Characteristics of non responders patients

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OP-9 Assessing the Burden and Budget Impacts of HCV Elimination Strategies in Uruguay Using Decision-Analytic Modeling

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Conflict of interest: Yes, Coalition For Global Hepatitis Elimination support the project