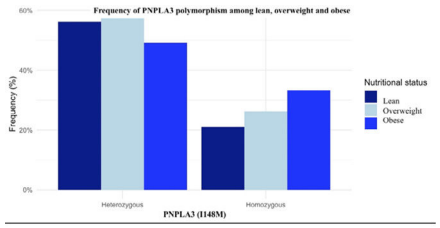
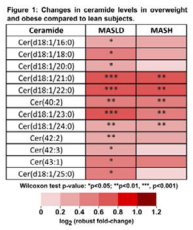
based on their BMI. The presence of the rs738409 polymorphism was examined using Sanger sequencing. Metabolomics was assessed using UHPLC-MS in a separate group of biopsy-proven MASLD patients. Statistical analyses of clinical data and genotypes encompassed Fisher's exact test, Chi-square test, Kruskal-Wallis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

Introduction and Objectives: Background: WHO aims for HCV elimination by 2030, targeting a 80% reduction in incidence and a 65% reduction in mortality, with 90% diagnosed and 80% treatment coverage compared to 2015. Uruguay, with a population of 3.4 million, has low HCV prevalence and universal treatment access, but testing and treatment rates are low. Objective: To assess the feasibility of HCV elimination and compare the burden and budget impacts of various testing strategies in Uruguay.

Patients / Materials and Methods: Methods: Disease burden and budget impact projections were generated using a decision-analytic model, The Hep C Elimination Tool, developed by Massachusetts General Hospital with support from the Coalition for Global Hepatitis Elimination and calibrated with Uruguayan parameters.

Results and Discussion: With 100% follow-up for confirmatory testing and treatment initiation, 42 strategies meet three elimination goals by 2030.

The strategy with the greatest death reductionuses a 30% annual screening rate and 80% treatment rate, requiring 3,220,000 people to be tested (800,000/annual from 2024-2026) and 20,000 treated (5,000/annual from 2024-2026) by 2030. This achieves 91% diagnosis and treatment coverage, with reductions in incidence of 89%, prevalence of 91%, decompensated cirrhosis of 74%, HCC of 46% and mortality of 56%, costing $121.63 million from 2022-2050.

The most gradual strategy uses a 15% annual screening rate and 70% treatment rate, requiring 3,190,000 people to be tested (400,000/annual from 2023-2029) and 19,035 treated (2,500/annual from 2024-2029) by 2030. This achieves 90% diagnosis and 85% treatment coverage, with reductions in incidence of 82%, prevalence of 85%, decompensated cirrhosis of 66%, HCC of 34% and mortality of 30%, costing $132.92 million from 2022-2050.

Conclusions: Uruguay can achieve WHO HCV elimination incidence goal and diagnosis and treatment targets by 2030. Mathematical modeling can inform policymakers about the impact of different interventions on HCV burden, supporting informed and cost-effective decision-making.

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OP- 10 - NON-STEROIDAL ANTI-INFLAMMATORY DRUGS: A COMPARATIVE ANALYSIS BETWEEN THE SPANISH AND LATINDILI NETWORKS

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Conflict of interest: No

Introduction and Objectives: Background: Non-steroidal anti-inflammatory drugs (NSAIDs) represent a frequent cause of drug-induced liver injury (DILI). Aim: To compare demographics, clinical characteristics and outcomes of NSAIDs-induced liver injury between the LATINDILI and the Spanish DILI Registries.

Patients / Materials and Methods: We analyzed 49 out of 468 LATINDILI cases (10,5%) and 82 out of 1254 Spanish DILI Registry cases (14%) induced by NSAIDs.

Results and Discussion: In Spanish DILI cases, ibuprofen (33%), diclofenac (18%) and nimesulide (11%), were the most frequent culprit drugs, while diclofenac (33%), nimesulide (29%), ibuprofen (18%) and etoricoxib (10%) were the most common offending agents in LATINDILI cases. Surprisingly, etoricoxib was far more frequent in LATINDILI (10%) than in the Spanish DILI Registry (1.2%). Females predominated in Latin American cases (73%) compared to Spanish cases (47%) (p=0.011). Also, there was a trend towards a higher hospitalization rate in Spanish cases (63%) compared to LATINDILI cases (43%). (p=0.057). Notably, Hy's law showed to have drug-specific predictive value, with ibuprofen, nimesulide and etoricoxib associated with fatal outcomes, whereas DILI due to other AINEs did not have a worse outcome. We separately analyzed cases due to the most frequent culprits in each registry (ibuprofen and diclofenac). Notably, one patient died and one patient underwent liver transplantation linked to ibuprofen in the Spanish DILI Registry, while no death nor liver transplants were recorded in the LATINDILI due to ibuprofen. Likewise, no fatal outcome related to diclofenac were observed in these registries

Conclusions: Differences in the incidence of DILI due to NSAIDs may reflect different prescribing patterns and public health policies in distinct countries. Ibuprofen can cause serious liver damage, and different doses in the OTC market and genetic factors may explain the differences in frequencies between registries. Hy's law prognostic performance varies between NSAIDs and is highest for nimesulide and ibuprofen. Etoricoxib DILI needs further investigation.

Table. Comparison of clinical presentation of DILI episode according to the most frequent individual AINEs registered in the Latin American DILI (LATINDILI) Network and the Spanish DILI Registry (at least 5 cases registered).

Culprit agents	n (%)	Age (y)	Pattern of DILI, n (%)			Female sex n (%)	Eosinophilia n (%)	Lymphopenia n (%)	Hy's law n (%)	True Hy's law (death/liver transplant) n (%)	nR-based Hy's law n (%)	True nR-based Hy´s law (death/liver transplant) n (%)
			Hep	Chol	Mix							
Spanish DILI Registry												
Ibuprofen	27 (33)	50±18	13 (48)	3 (11)	11 (41)	13 (48)	5 (20)	5 (22)	5 (20)	1 (20)	6 (24)	2 (33)
Diclofenac	15 (18)	60±20	14 (93)	1 (6.7)	0 (0)	6 (40)	1 (7.7)	2 (14)	7 (54)	0 (0)	7 (54)	0 (0)
Nimesulide	9 (11)	58±14	7 (78)	2 (22)	0 (0)	8 (89)	3 (33)	2 (25)	7 (78)	1 (14)	7 (78)	1 (14)
LATINDILI Network												
Diclofenac	16 (33)	55±11	11 (69)	5 (31)	0 (0)	10 (63)	2 (13)	3 (19)	6 (38)	0 (0)	6 (38)	0 (0)
Nimesulide	14 (29)	57±16	8 (57)	0 (0)	6 (43)	12 (86)	2 (14)	1 (7.1)	6 (50)	3 (50)	7 (58)	3 (43)
Ibuprofen	9 (18)	44±14	8 (89)	1 (11)	0 (0)	6 (67)	1 (13)	1 (13)	4 (50)	0 (0)	4 (50)	0 (0)
Etoricoxib	5 (10)	45±19	5 (100)	0 (0)	0 (0)	4 (80)	0 (0)	1 (20)	4 (80)	1 (25)	4 (80)	1 (25)

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OP- 11 Detection Strategy for Patients with Viral Hepatitis Using Laboratory Records of Blood Samples for HBsAg and HCV Antibodies: PANRELINK

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Conflict of interest: No