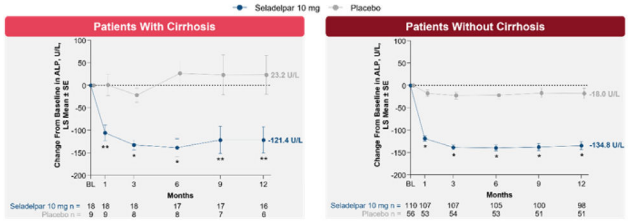
phosphatase (ALP) ≥1.67 × ULN, and total bilirubin ≤2 × ULN; they received seladelpar 10 mg or placebo (2:1 randomisation) for 12 months. Cirrhosis was defined by medical history, liver biopsy, transient elastography, laboratory findings, and radiological features. Safety and changes in laboratory parameters were assessed.

Results: Of 193 patients, 27 (14%) had Child-Pugh A compensated cirrhosis at baseline (18 seladelpar, 9 placebo). Mean ALP change was −121.4 U/L for seladelpar vs 23.2 U/L for placebo patients with cirrhosis, and −134.8 U/L for seladelpar vs −18.0 U/L for placebo patients without cirrhosis. Greater decreases in other laboratory parameters were observed with seladelpar vs placebo regardless of cirrhosis status. Adverse events with seladelpar vs placebo were similar in patients with and without cirrhosis. No patients with cirrhosis discontinued seladelpar due to adverse events. Elevations in alanine aminotransferase or aspartate aminotransferase of >3 × ULN occurred in 3 patients with cirrhosis.

Conclusions: Seladelpar reduced biomarkers of cholestasis and was overall safe and well tolerated in patients with PBC with or without cirrhosis.

Conflict of interest: Yes, Gilead Sciences, Inc.

Changes in ALP in Patients With PBC With or Without Cirrhosis at Baseline Treated With Seladelpar or Placebo in the RESPONSE Trial



*P<.0001. **P<.05

ALP, alkaline phosphatase; BL, baseline; LS, least squares; PBC, primary biliary cholangitis; SE, standard error.

https://doi.org/10.1016/j.aohep.2025.102052

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CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF HEPATOCELLULAR CARCINOMA IN A REFERRAL HOSPITAL IN LIMA, PERU

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Introduction and Objectives: Hepatocellular carcinoma (HCC) is the most common primary liver tumor (85–90%) and one of the leading causes of death among cirrhotic patients.

To determine the clinical and epidemiological characteristics of patients with HCC at a referral hospital in Lima, Peru.

Materials and Methods: A cross-sectional observational study including 282 patients diagnosed with HCC at the Liver Unit of HNERM-EsSalud between 2016 and 2023.

Results: 62% of patients were male, with a mean age of 65.4 years (range: 16–92). Cirrhosis was present in 78.4% of cases. The most common etiology was MASLD (52%), followed by hepatitis B (16.3%) and hepatitis C (13%). Liver function was classified as Child-Pugh A in 53%, B in 30%, and C in 17%. Only 40% were enrolled in a screening program. Tumor stage according to BCLC was: 0–A in 40%, B in 18.6%, C in 6%, and D in 33%. Serum AFP>200 ng/mL was observed in 45% of cases. Treatments included transarterial chemoembolization (21%), radiofrequency ablation (5.3%), surgery (15.6%), liver transplantation (6.4%), systemic therapy (6%), and palliative care (39%).

When comparing cirrhotic vs non-cirrhotic patients, hepatitis B was more frequent in the non-cirrhotic group (P<0.001), with larger tumors (11.1 cm vs. 5.3 cm, P<0.001), higher AFP levels, and lower screening rates.

Conclusions: MASLD was the leading cause of HCC overall, while hepatitis B predominated in non-cirrhotic patients. Only 40% underwent screening. Patients in early stages had access to better treatment options.

Conflict of interest: None

Variable	Non-cirrhosis (N=61)	Cirrhosis (N=221)	p-value
Age (mean, SD)	56.2 (18.1)	67.9 (9.8)	<0.001
Sex			0.733
Female	22 (36.1%)	85 (38.5%)	
Male	36(63.9%)	136 (61.5%)	
Etiology			0.001
MASLD	22 (36.1%)	125 (56.6%)	
Others	14 (23%)	39 (17.6%)	
HVB	19 (31.1%)	27 (12.2%)	
HVC	6 (9.8%)	30 (13.6%)	
Diabetes			<0.001
Yes	11 (18%)	93 (42.1%)	
No	50 (82%)	128 (57.9%)	
Hypertension			0.057
Yes	18 (29.5%)	95 (43%)	
No	43 (70.5%)	126 (57%)	
Coronary artery disease			0.193
Yes	0 (0%)	6 (2.7%)	
No	61 (100%)	215 (97.3%)	
Renal disease			0.361
Yes	2 (3.3%)	14 (6.3%)	
No	59 (96.7%)	215 (97.3%)	
Diagnosis exam for HCC			<0.001
Surveillance	4 (6.6%)	108 (48.9%)	
Symptoms	57 (93.4%)	113 (51.1%)	
Diagnosis methods			<0.001
Image	28 (45.9%)	204 (92.3%)	
Biopsy	35 (54.1%)	17 (7.7%)	
Tumor diameter (mean, SD)	11.1 (6)	5.8 (3.7)	<0.001
Nodules number			0.074
<=3	47 (77%)	191 (86.4%)	
>3	14 (23%)	30 (13.6%)	
AFP			0.015
<20	12 (19.7%)	66 (29.9%)	
20-200	13 (21.3%)	65 (29.4%)	
200-400	3 (4.9%)	20 (9%)	
>400	33 (54.1%)	70 (31.7%)	
Treatment			<0.001
Palliative	24 (39.3%)	86 (38.9%)	
TACE	0 (0%)	59 (26.7%)	
RFA	1 (1.6%)	14 (6.3%)	
Systemic	7 (11.5%)	10 (4.5%)	
Surgery	23 (37.7%)	23 (10.4%)	
Liver transplant	0 (0 %)	16 (7.2%)	
Others	6 (9.8%)	13 (5.9%)	

https://doi.org/10.1016/j.aohep.2025.102053

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IMPORTANCE OF P450 POLYMORPHISM IN THE DEVELOPMENT OF DILI/HILI: HISTOLOGICAL AND BIOCHEMICAL FINDINGS

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Introduction and Objectives: Drug-induced liver injury (DILI) and herb-induced liver injury (HILI) represent diagnostic and prognostic challenges in hepatology. Objective: To evaluate histological, epidemiological, biochemical variables and the prevalence of cytochrome P450 (CYP450) genotypes in individuals with DILI/HILI at a hepatotoxicity clinic.

Materials and Methods: Cross-sectional study with individuals who developed DILI/HILI and underwent liver biopsy.

Results: Sample comprised 58 individuals, divided into 2 groups: those who developed ALF (34) and those who did not (24). Mean age 38.71 (SD 14.58), 79.3% female. Hepatocellular biochemical pattern: 70.7%, mixed 12.1%, cholestatic 17.2%. The ALF group did not present a cholestatic pattern. Most frequent drugs: antituberculosis (8), nimesulide (5), diclofenac (4). Regarding biochemistry, in the group without ALF, comparing presence of the main drug with or without CYP450 metabolism: BT 5.32 mg/dL vs 4.01; ALT 289.5 U/L vs 274; AST 316 U/L vs 272.5; INR 1 vs 1; AST/ALT 1.07 vs 0.91. In the ALF group: BT 18.75 vs 29.94 mg/dL; ALT 885 vs 474.5 U/L; AST 1350 vs 498.5 U/L; AST/ALT 1.37 vs 0.79. Hy's law applied to 100% of ALF cases. Patients using two or more concomitant drugs showed worse biochemical and histological findings. Most frequent CYPs among non-ALF: CYP3A4 20.68%, CYP2C9 8.62%, CYP2D6 6.89%; among ALF: CYP3A4 31.03%, CYP2C9 15.51%, CYP2A2 8.62%. Histological findings: massive/submassive necrosis was present in 85.29% of ALF patients, mainly in those with CYP metabolism. Fibrosis was more frequent in the group without progression to ALF (9 vs 3).

Conclusions: Hepatic metabolism by CYP450 is associated with more severe DILI/HILI, including higher frequency of hepatic necrosis and elevated biochemical values. Recognizing the metabolic profile of implicated drugs may help predict injury severity and guide earlier, individualized treatment strategies.

Conflict of interest: None

https://doi.org/10.1016/j.aohep.2025.102054

Variable	DILI without ALF (n = 24)		DILI with ALF (n = 34)		p
	CYP450 (n=16)	Non-CYP (n=8)	CYP450 (n=28)	Non-CYP (n=6)	
Age (years), mean (SD)	39.56 (14.23)	48.75 (13)	32.29 (12.5)	40.5 (22.28)	>0,05
Female sex, n (%)	13 (22.41)	6 (10.34)	22 (37.93)	6 (10.34)	>0,05
INR, median (IQR)	1 (0.99–1.06)	1 (0.97–1.3)	3.74 (2.2–5.25)	3.48 (2.2–9.08)	<0,05
BT (mg/dL), median (IQR)	5.32 (0.99–11.59)	4.01 (0.6–15.97)	18.75 (10.67–26.49)	26.94 (21.71–28.73)	>0,05
ALT (U/L), median (IQR)	289.5 (160.75–608.5)	274 (219–635)	885 (593–1563)	474.5 (455.75–2138)	<0,05
AST (U/L), median (IQR)	316 (110–873)	272.5 (152.7–556.5)	1350 (552–3450)	498.5 (350.5–2892.75)	<0,05
Liver injury pattern, n (%):					
Hepatocellular	8 (13.7)	3 (5.17)	24 (41.37)	6 (10.34)	<0,05
Cholestatic	7 (12)	0 (0)	0 (0)	0 (0)	<0,05
Mixed	2 (3.44)	4 (6.89)	4 (6.89)	0 (0)	<0,05
AST/ALT ratio, median (IQR)	1.07 (0.51–1.52)	0.91 (0.57–1.16)	1.37 (0.75–2.38)	0.79 (0.54–2.2)	<0,5
Hy's Law criteria met, n (%):	11 (18.9)	4 (6.89)	28 (48.27)	6 (10.34)	<0,05
Concomitant medications ≥2, n (%)	9 (15.51)	6 (10.34)	20 (34.48)	3 (5.17)	>0,05
Concomitant CYP450-metabolized drugs, n (%)	10 (17.24)	3 (5.17)	10 (17.24)	2 (3.44)	>0,05
Most frequent CYP450 isoenzymes, n (%):					
CYP3A4	12 (20.68)	—	18 (31.03)	—	>0,05
CYP2C9	5 (8.62)	—	9 (15.51)	—	>0,05
CYP2D6	4 (6.89)	—	2 (3.44)	—	>0,05
CYP3A5	1 (1.72)	—	2 (3.44)	—	>0,05
CYP2C19	3 (5.17)	—	4 (6.89)	—	>0,05
CYP2E1	2 (3.44)	—	3 (5.17)	—	>0,05
CYP1A2	1 (1.72)	—	5 (8.62)	—	>0,05
Most frequent causative drugs:	Chlorpromazine (2), nimesulide (2)	Amoxicillin–clavulanate (2)	Diclofenac (4), nimesulide (3), antituberculosis drugs (8),	methyldopa (3)	
Histological findings, n (%):					
Chronic hepatitis	3 (5.17)	1 (1.71)	1 (1.71)	1 (1.71)	>0,05
Active chronic hepatitis	3 (5.17)	1 (1.71)	2 (3.44)	1 (1.71)	>0,05
Acute cholestasis	5 (8.62)	1 (1.71)	6 (10.34)	1 (1.71)	>0,05
Chronic cholestasis	1 (1.71)	0 (0)	0 (0)	0 (0)	>0,05
Cholestatic hepatitis	4 (6.89)	0 (0)	2 (3.44)	1 (1.71)	>0,05
Type of necrosis, n (%):					
Massive/submassive necrosis	0 (0)	0 (0)	24 (41.37)	5 (8.62)	>0,05
Zonal/focal necrosis	5 (8.62)	4 (6.89)	4 (6.89)	1 (1.71)	<0,05
Other histological findings, n (%):					
Steatosis	1 (1.71)	0 (0)	3 (5.17)	0 (0)	>0,05
Fibrosis	9 (15.51)	1 (1.71)	3 (5.17)	0 (0)	<0,05
Siderosis	2 (3.44)	1 (1.71)	4 (6.89)	3 (5.17)	>0,05
Mononuclear infiltrate	14 (24.13)	4 (6.89)	18 (31.03)	5 (8.62)	>0,05
Interface activity	4 (6.89)	1 (1.71)	0 (0)	0 (0)	<0,05
Hepatocyte ballooning	7 (12)	2 (3.44)	2 (3.44)	0 (0)	<0,05
Ductular reaction/proliferation	10 (17.24)	3 (5.17)	7 (12)	1 (1.71)	>0,05