their enzymes to alternative pathways for ammonia detoxification, disrupting normal energy metabolism.

Materials and Methods: Adult male Sprague Dawley rats were randomly assigned to a control group on a standard diet (2.93 kcal/g, n=10), an intervention group on a high-fat diet deficient in choline (MASLD, HDCF, 4.3 kcal/g, n=10), and two treatment groups, MASLD +NAC (n=12) and MASLD+LOLA (n=12), over a period of 16 weeks.

Results: In MASLD, there was an increase in the expression of D3, colocalized with M1 macrophages and TR beta protein levels, while MCT8 levels remained unchanged. Additionally, mitochondrial respiration decreased, and no effects were observed with treatments. Furthermore, Glutamate Dehydrogenase (GDH) activity diminished, whereas α-Ketoglutarate Dehydrogenase (α-KGDH) activity increased. It was also determined that Grp78 (decreased by 74%) and Grp75 (increased by 60%) are regulated by T3 and are endoplasmic reticulum (ER) chaperones meaning ER stress.

Conclusions: Our study corroborates the interaction between TH metabolism and compensatory mechanisms that counteract elevated ammonia levels, as well as the enzymes regulating this process in MASLD. Both NAC and LOLA demonstrated potential in correcting TH metabolism and enhancing ammonia detoxification in MASLD, which may help alleviate symptoms or slow the progression of the disease.

Conflict of interest: None

https://doi.org/10.1016/j.aohep.2025.102050

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EFFICACY AND SAFETY OF SELADELPAR IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS PREVIOUSLY TREATED WITH FIBRATES OR OBETICHOLIC ACID

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Introduction and Objectives: Seladelpar was evaluated as monotherapy or with ursodeoxycholic acid in RESPONSE (NCT04620733) among patients with primary biliary cholangitis. Patients completing RESPONSE could roll over into ASSURE (NCT03301506).

Here, we present 18-month (M) data (6M of ASSURE) in patients with or without prior use of fibrates or obeticholic acid (OCA) continuing into ASSURE from RESPONSE.

Patients and Methods: Patients received oral seladelpar 10 mg or placebo during RESPONSE, followed by open-label seladelpar in ASSURE. Fibrates/OCA were prohibited during RESPONSE. Analyses included patients with or without prior fibrates/OCA use, categorized by RESPONSE assignment: continuous seladelpar or crossover from placebo. Efficacy included the proportion of patients achieving a composite biochemical response (CBR; ALP $<1.67 \times$ ULN, ALP decrease $\geq$15%, and total bilirubin $\leq$ULN). Safety evaluations included adverse events (AEs).

Results: Among patients who continued into ASSURE from RESPONSE (n=158), 16 continuous seladelpar and 11 crossover patients reported prior use of fibrates/OCA (n=27; 17%); 88 continuous seladelpar and 43 crossover patients reported no prior use of fibrates/OCA (n=131; 83%). At 18M, 9/15 (60%) continuous seladelpar patients with prior fibrates/OCA use achieved a CBR vs 54/87 (62%) patients without prior fibrates/OCA use. Among crossover patients, 7/11 (64%) patients with prior fibrates/OCA use vs 32/41 (78%) patients without prior fibrates/OCA use achieved a CBR at 6M of ASSURE. From ASSURE initiation to 6M, AE incidence was similar across all patients, regardless of prior fibrates/OCA use; no treatment-related serious AEs were reported.

Conclusions: Interim results show seladelpar achieved comparable, sustained biochemical responses and favorable safety irrespective of prior fibrates/OCA use.

Conflict of interest: Yes, Gilead Sciences, Inc.

https://doi.org/10.1016/j.aohep.2025.102051

#129

EFFICACY AND SAFETY OF SELADELPAR IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS AND COMPENSATED CIRRHOSIS IN THE PHASE 3 PLACEBO-CONTROLLED RESPONSE TRIAL

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Introduction and Objectives: In the Phase 3 RESPONSE trial (NCT04620733), seladelpar, a first-in-class delpar (selective peroxisome proliferator–activated receptor delta agonist), significantly improved biomarkers of cholestasis in patients with primary biliary cholangitis (PBC) over 12 months vs placebo. More patients with cirrhosis met the primary endpoint in the seladelpar arm (39%) vs placebo (22%).

We now report data on additional biochemical results and safety in patients with or without cirrhosis in RESPONSE.

Patients and Methods: Eligible patients had an inadequate response or intolerance to ursodeoxycholic acid, alkaline

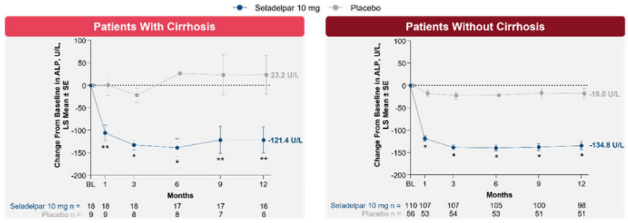
phosphatase (ALP) ≥1.67 × ULN, and total bilirubin ≤2 × ULN; they received seladelpar 10 mg or placebo (2:1 randomisation) for 12 months. Cirrhosis was defined by medical history, liver biopsy, transient elastography, laboratory findings, and radiological features. Safety and changes in laboratory parameters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

#131

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.