AASLD November 13-16, 2020
The Liver Meeting®
Digital Experience

THE BEST OF THE LIVER MEETING® 2020

# Cholestatic and Autoimmune Liver Diseases

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

## About the program:

*Best of The Liver Meeting 2020* was created by the Scientific Program Committee for the benefit of AASLD members, attendees of the annual conference, and other clinicians involved in the treatment of liver diseases. The program is intended to highlight some of the key oral and poster presentations from the meeting and to provide insights from the authors themselves regarding implications for patient care and ongoing research.

| Scientific Program Committee | |
|---|---|
| **Chair** | *Jorge A. Bezerra, MD, FAASLD* |
| **Co-Chair** | *Meena B. Bansal, MD, FAASLD* |
| **President-Elect** | *Raymond T. Chung, MD, FAASLD* |
| **Senior Councilor** | *Laurie D. DeLeve, MD, PhD, FAASLD* |
| **Annual Meeting Education Committee** | *Grace L. Su, MD, FAASLD* |
| **Basic Research Committee** | *Harmeet Malhi, MD, MBBS, FAASLD* |
| **Clinical Research Committee** | *Kymberly Watt, MD* |
| **CME Committee** | *Joseph K. Lim, MD, FAASLD* |
| **Hepatology Associates Committee** | *Elizabeth K. Goacher, PA-C, MHS, AF-AASLD* |
| **Surgery and Liver Transplantation Committee** | *Bijan Eghtesad, MD, FAASLD* |
| **Training and Workforce Committee** | *Janice Jou, MD, MHS, FAASLD* |

## Use of these slides:

# Outcomes of pregnancy in autoimmune hepatitis: a population-based study

## Aim

To determine whether AIH in pregnancy increases the risk of adverse maternal and perinatal outcomes

## Methods

Retrospective study from US National Inpatient Sample (2012-16) comparing outcomes in pregnancies with AIH (n=935) vs other chronic liver diseases (CLD) (n=120,00) or no CLD in pregnancy (n=18,474,310). Regression models adjusted for age, race, multiple gestation, pre-pregnancy metabolic disease, and cirrhosis.

**Table. AIH and Adverse Maternal and Perinatal Outcomes: Adjusted Analyses**

| | AIH vs Other CLD | | AIH vs no CLD | |
|---|---|---|---|---|
| | AOR*, 95% CI | p value | AOR*, 95% CI | p value |
| **Maternal Outcomes** | | | | |
| Hypertensive complications (pre-eclampsia, eclampsia, and/or HELLP syndrome) | **1.77 (1.00-3.17)** | **0.05** | **2.35 (1.34-4.11)** | **0.003** |
| Gestational DM | **2.23 (1.47-3.38)** | **<.001** | **2.40 (1.61-3.60)** | **<.001** |
| **Perinatal Outcomes** | | | | |
| Pre-term birth (<37 weeks) | 1.20 (0.69-2.06) | 0.52 | **2.02 (1.17-3.49)** | **0.01** |

*Abbreviations: autoimmune hepatitis (AIH), chronic liver disease (CLD), diabetes mellitus (DM), hypertension (HTN), hemolysis, elevated liver tests, low platelets (HELLP)*
**Adjusted for age, race, multiple gestation, obesity, pre-existing HTN, pre-existing DM, pre-existing hyperlipidemia, and cirrhosis (when comparing AIH to other CLD)*

## Main Findings

AIH prevalence in pregnancy remained stable in recent years. AIH increased the risk for hypertensive complications of pregnancy, gestational diabetes, and pre-term birth, but not maternal or perinatal mortality (see Table).

## Conclusions

- AIH was associated with notable maternal and perinatal risks though whether risks are influenced by AIH treatment and/or disease activity warrants further evaluation.
- AIH did not increase maternal or perinatal mortality.

Wang CW, et al., Abstract 99

# The association of UDCA treatment with long-term outcome and biliary tract cancer in Japanese patients with primary sclerosing cholangitis

## Aim

To elucidate whether UDCA treatment was associated with long-term outcome (all-cause death or liver transplantation [LT]) and development of biliary tract cancer (BTC) in a well-characterized Japanese cohort of PSC patients

## Methods

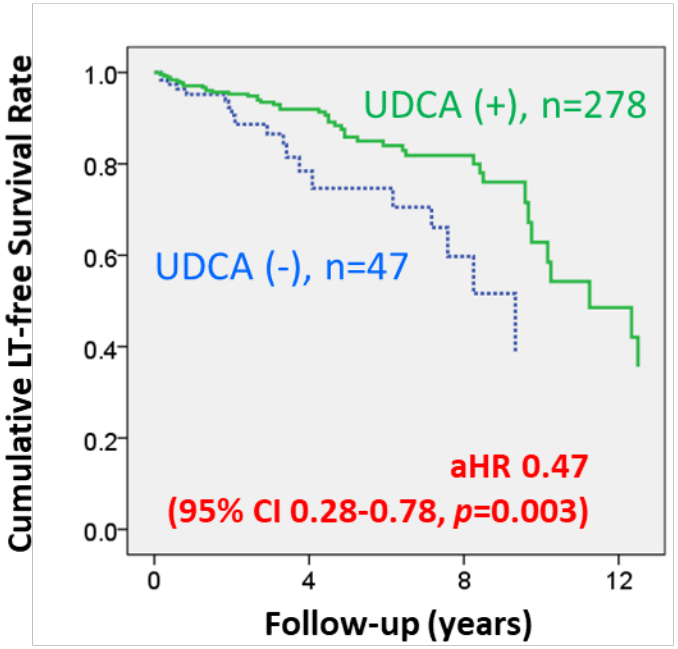
325 patients with PSC treated with UDCA (n=278) and without UDCA (n=47) were analyzed retrospectively with Cox-regression model and IPTW model, adjusted for covariates.

## Conclusions

UDCA treatment was significantly associated with an improvement in LT-free survival in this Japanese PSC cohort. While UDCA was likely to be associated with a reduction of biliary tract cancer, it was not consistently significant.

Arizumi T, et al., Abstract 100

**LT-free survival in UDCA (+) vs UDCA (-) (covariate-adjusted)**




| | All-cause Death or LT | | Development of BTC | |
|---|---|---|---|---|
| | aHR | P | aHR | P |
| Cox Regression Model | 0.47 (0.28-0.78) | 0.003 | 0.32 (0.14-0.78) | 0.012 |
| IPTW Model | 0.43 (0.25-0.75) | 0.020 | 0.42 (0.16-1.10) | 0.100 |

# Fenofibrate increases bile acid glucuronidation & reduces bile acid toxicity in patients with PBC and PSC who are partial responders to ursodiol

## Hypothesis

Fenofibrate, a PPARα agonist, upregulates bile acid (BA) glucuronidation, which reduces BA toxicity in patients with PBC and PSC who are partial responders to Ursodiol monotherapy.

## Methods

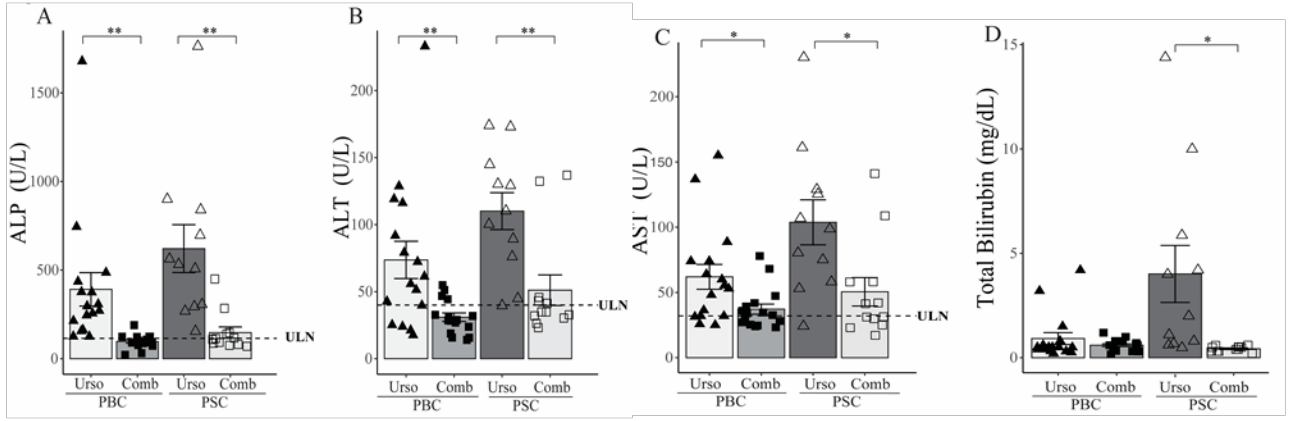
Serum BA and BA-glucuronide profiles from adult patients with PBC and PSC receiving Ursodiol monotherapy with ALP ≥1.5 x ULN ± fenofibrate by mouth were analyzed by LC-MS/MS.

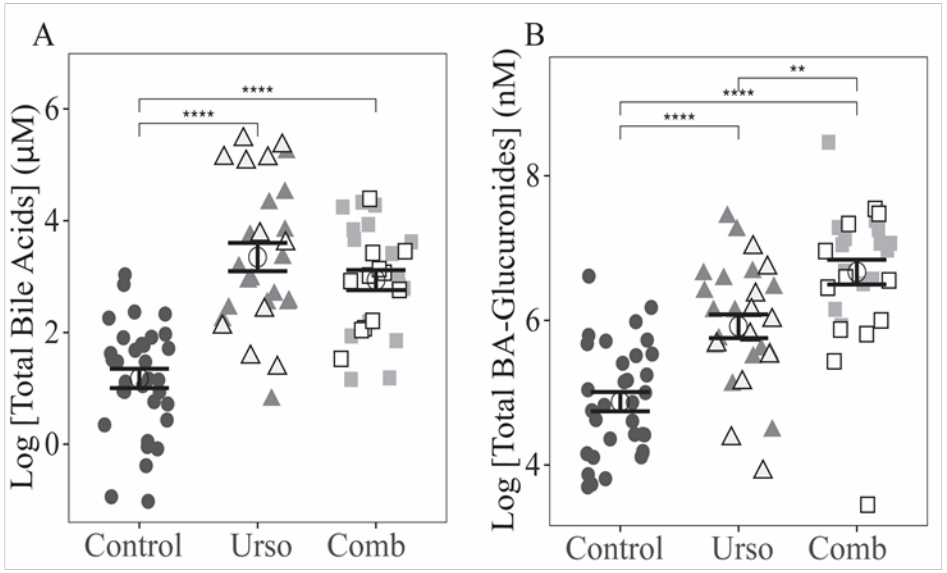
## Main Findings

Combination therapy with fenofibrate and Ursodiol reduces elevated liver enzyme levels, reduces total serum BAs, and increases total serum BA-glucuronides in patients with PBC and PSC who have an incomplete response to Ursodiol monotherapy.

## Conclusions

Addition of fenofibrate therapy increases BA-glucuronidation as a PPARα-mediated mechanism to reduce the toxicity of serum BAs in patients with PBC and PSC who are incomplete responders to Ursodiol monotherapy.




Gallucci GM, et al., Abstract 101

# EXerCise Intervention in cholesTatic livEr Disease

## Objective

Feasibility and efficacy of a home-based exercise program (HBEP) to attenuate fatigue associated with PBC

## Study

- Single-arm, open-label trial
- PBC with moderate-severe fatigue (PBC40 fatigue score >33)
- Endpoint: median reduction in fatigue score ≥5

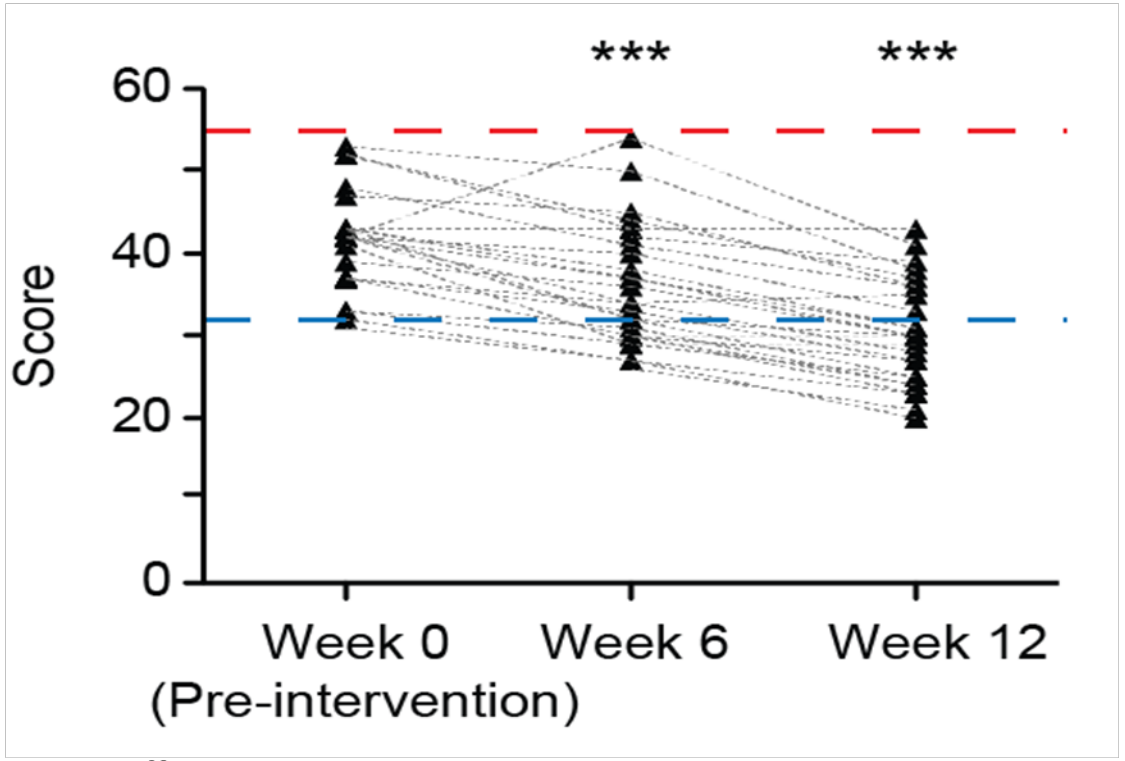
## Results (interim findings; n=25 participants)

- Significant reduction in PBC-associated fatigue (see Figure 1)
- N=23/25 attained the primary endpoint
- N=19/25 attained fatigue scores akin to the control population

## Conclusion

HBEP is safe, feasible, and effective in attenuating fatigue in PBC.

**Figure 1. Changes in Fatigue Domain of PBC-40**




**Key**

*** Friedman matched pairs test w/post-hoc correction $P<0.001$

Highest entry self-reported fatigue score

Lowest entry self-reported fatigue score

Freer A, et al., Abstract 102

# ENHANCE: safety and efficacy of seladelpar in patients with primary biliary cholangitis

## Aim

Evaluate the efficacy, safety, and tolerability of seladelpar, a selective PPPA-delta agonist, in the treatment of patients with PBC

## Methods

- Phase 3, placebo-controlled, randomized study;
  PBC patients with an inadequate response or intolerance to UDCA
- End-point: ALP < 1.67 × ULN; ≥ 15% decrease in ALP; Total Bilirubin ≤ ULN

## Main Findings

**Seladelpar 10 mg after 3 months of treatment resulted in**:

- 78% of patients with composite biochemical response and achieving primary study endpoint
- Statistically significant effect on ALP normalization
- Statistically significant reduction in pruritus
- Generally safe and well tolerated

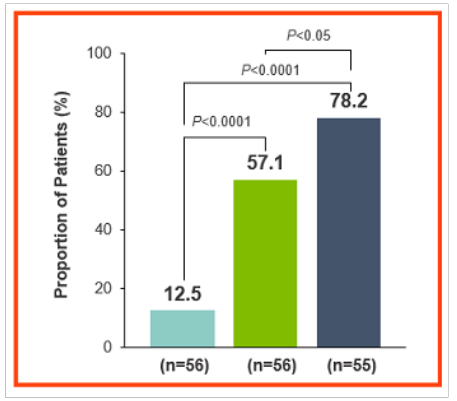
## Conclusions

Seladelpar demonstrated biochemical efficacy, improved pruritus, and was generally safe and well tolerated.

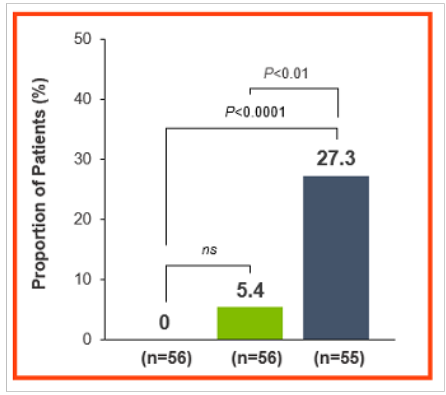
Hirschfield GM, et al., Abstract LO11

**After 3 months of treatment**

**78% met composite endpoint**

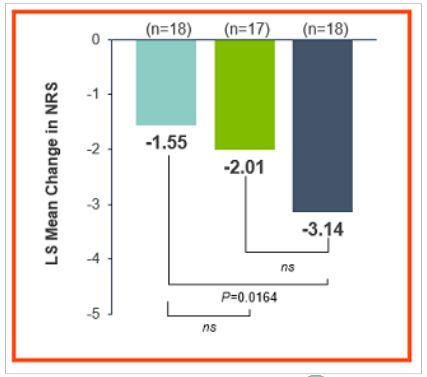



**27% of patients normalized ALP**



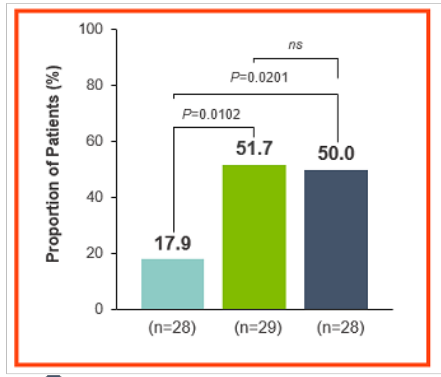

**Significant improvements in pruritus**

Patients with baseline NRS ≥4




**50% normalized ALT**

Patients with baseline ALT ≥ULN




Placebo 5 mg 10 mg

# Saroglitazar for primary biliary cholangitis (PBC)

## Objective

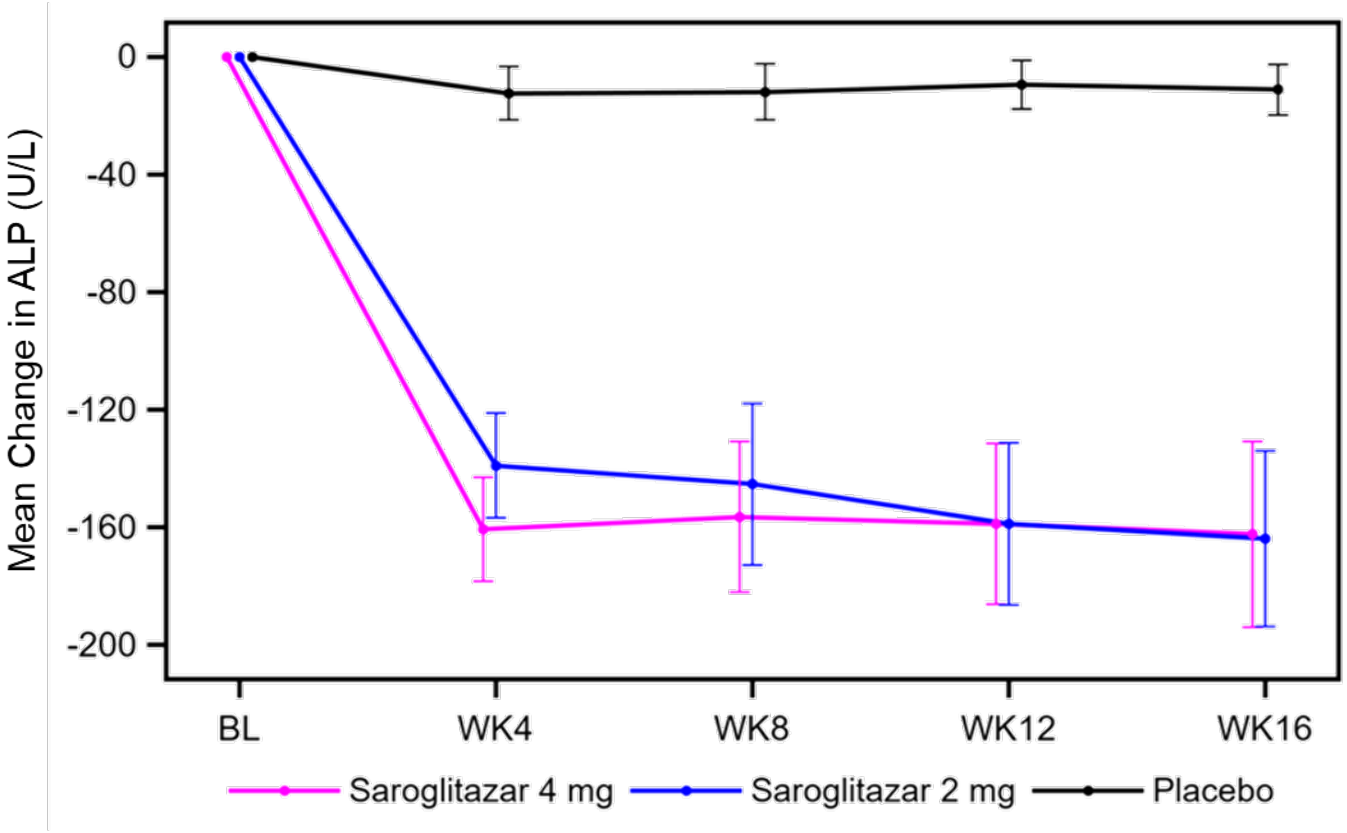
Evaluate safety, tolerability, and efficacy of saroglitazar in patients with PBC

## Methods

- Double-blind, prospective trial comparing the efficacy of Saroglitazar 2 and 4 mg in patients with PBC
- Patient population studied – UDCA unresponsive with ALP ≥1.67 × ULN

## Main Findings

Saroglitazar 4 mg: (mean = -163.3 U/L, SE = 25.1, $p<0.001$) and 2 mg (mean = -155.8 U/L, SE = 24.4, $p<0.001$) resulted in statistically significant drop in ALP compared to placebo (mean = -21.1 U/L, SE = 28.9) (See Figure).




## Conclusions

Saroglitazar at 2 and 4 mg daily resulted in *rapid and sustained* improvements in ALP.

Vuppalanchi R, et al., Abstract LO12

AASLD November 13-16, 2020
The Liver Meeting®
Digital Experience

THE BEST OF THE LIVER MEETING® 2020

# Cholestatic and Autoimmune Liver Diseases

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES