Change in Lipids: Characteristics and Response to Obeticholic Acid (OCA) in TARGET-PBC, a Diverse, Large United States (US) Real-world Cohort

Cynthia Levy[1], Marlyn J. Mayo[2], Elizabeth J. Carey[3], Ester C. Little[4], W. Ray Kim[5], Karen Deane[6], Richard Zink[6], Robert Sandefur[6], Christopher L. Bowlus[7]

[1]Division of Gastroenterology and Hepatology, University of Miami, Schiff Center for Liver Diseases, Miami, FL; [2]Division of Gastroenterology and Hepatology, University of Texas Southwestern, Dallas, TX; [3]Divison of Gastroenterology and Hepatology, Mayo Clinic, Phoenix, AZ; [4]Divison of Gastroenterology and Hepatology, Advanced Liver Disease and Transplant Institute, Banner- University of Arizona, Phoenix, AZ; [5]Division of Gastroenterology and Hepatology, Stanford University Medical Center, Stanford, CA; [6]TARGET PharmaSolutions, Inc., Chapel Hill, NC; [7]Divison of Gastroenterology and Hepatology, University of California Davis, Sacramento, CA

INTRODUCTION

- Hyperlipidemia is often associated with primary biliary cholangitis (PBC) but does not appear to increase cardiovascular risk.
- Use of obeticholic acid (OCA) in PBC has been associated with a reduction in total cholesterol (TC) primarily related to lowering high-density lipoproteins (HDL).
- A mild increase in low-density lipoproteins (LDL) is also observed in patients with PBC treated with OCA.
- The aim of this study was to determine the impact of OCA on lipid profile when treating patients who have PBC in a real-world setting.

METHODS

Cohort

- TARGET-PBC is an ongoing longitudinal, observational cohort of patients with PBC managed according to local practice standards at 35 academic and community sites in the United States.
- Participating clinics provided redacted medical records (structured and unstructured data) from consented patients. Patient narratives, laboratory, pathology, and imaging data were extracted and stored in a secured database. Patient reported outcome (PRO) measures were also collected approximately ever 6 months. Patients contributed blood samples to a biospecimen repository for biomarker validation and translational research.

Study Population

- Our study population included 108 patients enrolled in TARGET-PBC between November 9, 2016 and February 14, 2019 and treated with OCA for at least three months.

Outcome Measure

- Statin use was estimated as any documented use of a statin medication from the time of enrollment through February 14, 2019 or in the three years prior to enrollment.
- Cholesterol measurements from the medical record were ascertained before statin use and at the last documented visit during the follow up period.

Statistical Analysis

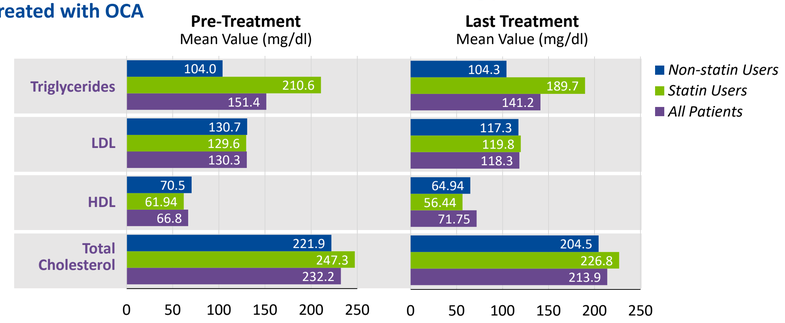
- The mean percent change in lipid values among patients treated with OCA was compared by statin and cirrhosis status use using chi squared tests.

Table 1. Descriptive characteristics

Patient Characteristics		Patients on OCA > 3 months (N=108)
Age at Study Entry, *Mean (SD)*		58.2 (10.89)
Length of OCA treatment months, *Mean(SD)*		18.6 (11.80)
Min-Max, *months*		4-70
Gender, *N (%)*	***Female***	99 (91.7)
	Not Available	-
Race, *N (%)*	***White***	87 (80.6)
	Black	5 (4.6)
	Other	5 (4.6)
	Not Available	11 (10.2)
Ethnicity, *N (%)*	***Hispanic or Latino***	27 (25.0)
	Not Available	11 (10.2)
Autoimmune Overlap Syndrome, *N (%)*		12 (11.1)
History of Cirrhosis, *N (%)*		53 (49.1)
Statin Use, *N (%)*	***Any Use***	38 (35.2)
	Non User	70 (64.8)
	Not Available	-

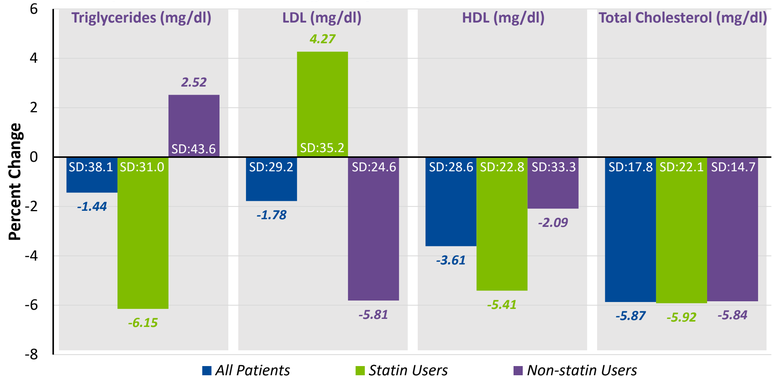
RESULTS

Figure 1. Distribution of mean cholesterol values among patients with PBC who were treated with OCA



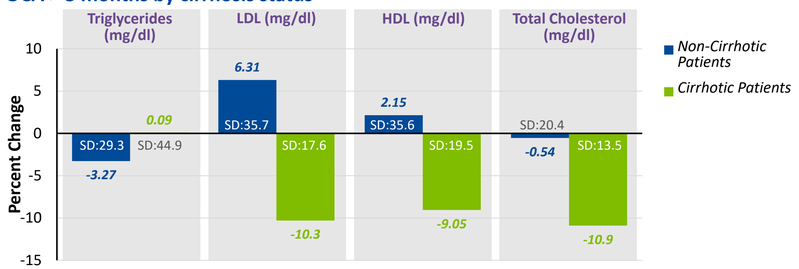
Sample size includes 38 patients on OCA>3 months with available cholesterol measures

Figure 2. Change in mean cholesterol values among patients with PBC ever on OCA for > 3 months (based on data from Figure 1)



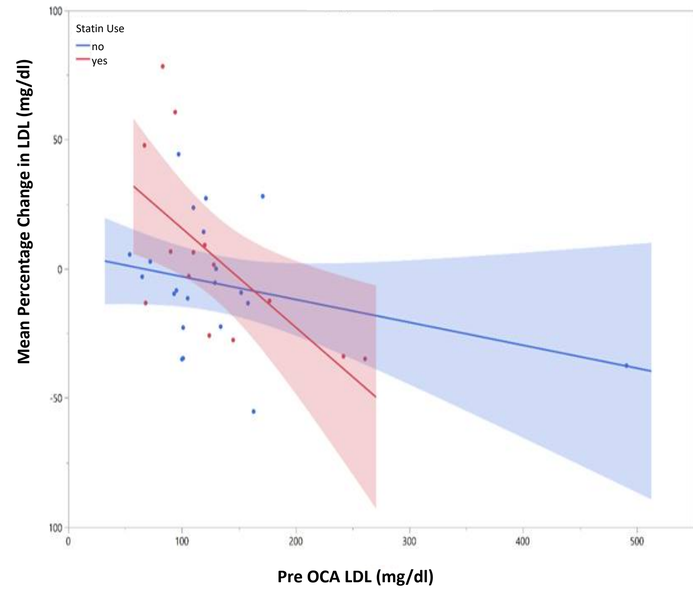
Sample size includes 38 patients on OCA>3 months with available cholesterol measures. Percent change is from the pre-OCA measurement to the last available on treatment lipid measurement.
Percent Change in LDL had a significant interaction between statin group and baseline LDL value: P=0.04

Figure 3. Change in mean cholesterol values among patients with PBC ever treated with OCA > 3 months by cirrhosis status



Sample size includes 108 patients on OCA>3 months
Percentage Change in Total Cholesterol had a significant interaction between cirrhosis status and baseline value: p=0.04
Percentage Change in LDL had a significant interaction with cirrhosis status and baseline value: p=0.05

Figure 4. Mean change in LDL by pre-OCA LDL value stratified by statin use among patients with PBC on OCA > 3 months



CONCLUSIONS

- **Use of OCA was associated with a reduction in HDL and total cholesterol**
- **The difference in means of the percentage change in LDL among statin users compared to non statin users was dependent on the baseline LDL value. Assuming this interaction was not significant ,the mean change in LDL was significantly greater for patients treated with OCA who were statin users compared to patients not using a statin medication**
- **The difference in means of the percentage change in LDL and Total Cholesterol among patients with cirrhosis compared to patients without cirrhosis was dependent on the baseline values. Assuming this interaction was not significant, OCA was associated with an increase in LDL among patient without cirrhosis, but rather a decrease in LDL among patients with cirrhosis possibly related to natural history of disease**
- **Additional studies are required to understand the impact of OCA on the lipid profile of patients.**

Acknowledgements and Disclosures: TARGET-PBC is a study sponsored by Target PharmaSolutions (TPS). TPS is a real-world clinical data company based in Durham, NC. The authors would like to thank all the investigators, participants and research staff associated with TARGET-PBC. ClinicalTrials.gov Identifier:NCT02932449

Dr. Levy consults for Target, Blade, Pliant and Cara Therapeutics. She received research grants from Gilead, Intercept, Tobira, NGM, Shire, HighTide, Durect, Novartis, CymaBay, GlaxoSmithKline, Enanta, Genkyotek, Genfit, Zydus and Lilly. She received royalties from Uptodate.