Background and Aims: Obeticholic acid (OCA), a potent and selective FXR agonist, has been shown to improve fibrosis in NASH patients in a pivotal Phase 3 study (REGENERATE). As part of the OCA development program, a study in patients (pts) with NASH evaluated the effect of OCA on liver function improvement using the HepQuant methodology. HepQuant measures the hepatic extraction of exogenously administered labeled cholate as a marker of liver function, which has been correlated to clinical outcomes using a Disease Severity Index (DSI). Based on prior studies of the relationship of DSI to probability of varices, a 2-point decrease in DSI is considered clinically meaningful. The aim of this analysis was to measure liver function in NASH patients with fibrosis after 3 months of OCA treatment.
Method: 51 pts were randomized 1:2:2 to placebo, OCA 10 mg, or OCA 25 mg QD for 85 days. Labeled cholate was administered intravenously and orally on Day -1 (baseline), 8, and 85 for HepQuant assessment.
Results: 50 pts, primarily white with median age 55yrs and BMI 35kg/m2 completed Day 85. 45 pts had a DSI at baseline (27% F1, 62% F2/3, 11% F4); 43 pts had both a baseline and Day 85 DSI assessment. The mean baseline DSI±SD (n) was for F1 16.4±3.8 (n=12), F2/3 19.0±4.6 (n=28), and F4 22.1±6.7 (n=5). The mean baseline DSI score for all pts (F1-F4) was consistent with an increased likelihood for varices based on previous results in NASH and HCV pts1. OCA treatment improved hepatic function as evidenced by the number of responders (>2-point decrease) and median decrease in DSI at Day 85 (Table). No unexpected safety findings were observed.
Conclusion: This is the first demonstration of OCA eliciting a dose-dependent clinically significant improvement in liver function in NASH. These results are consistent with the dose-dependent reversal of fibrosis observed in REGENERATE and further support the efficacy of OCA treatment in pts with fibrosis due to NASH.
Figure:
Reference: 1. Helmke S, et al. Presented at NASH Biomarkers. 2017 (Poster #15)

	Placebo	OCA 10 mg	OCA 25 mg
	F2/F3		
Responders	0% (0/5)	36% (4/11)	73% (8/11)
ΔDSI (Median)	-0.65	0.78	-3.81
	All (F1-F4)		
Responders	10% (1/10)	44% (7/16)	59% (10/17)
ΔDSI (Median)	-1.07	-1.17	-2.78