NASH patients with fibrosis stages 2 and 3 were randomized (1:1:1) to placebo (N=311), OCA 10 mg (N=312), or OCA 25 mg (N=308) once daily. Changes in FM (N=604), FM VCTE (N=604), and FAST (N=391) were analyzed using a mixed-effect repeated measures model (MRMM), with factors of treatment, baseline, visit, visit-by-treatment interaction, and stratification. Least square means and p-values were based on MMRM.

At baseline, no significant differences were observed in scores across treatment groups (figure 1). Patients with stage 3 fibrosis at baseline had higher scores than those with stage 2 fibrosis. OCA-treated patients experienced improvements in FM, FM VCTE, and FAST at Month 6 through Month 18. No improvements were observed with placebo (figure 1).

OCA treatment resulted in early and sustained improvements in non-invasive assessments of fibrosis in NASH. Improvements in FM and FM VCTE are consistent with OCA's anti-fibrotic effect, while improvements in FAST are consistent with amelioration of NASH inflammation and fibrosis.

In an 18-month interim analysis of REGENERATE, obeticholic acid (OCA) improved steatohepatitis and fibrosis based on surrogate endpoints of liver histology in patients with non-alcoholic steatohepatitis (NASH). Liver biopsy has several limitations, and development of non-invasive tools for NASH diagnosis and monitoring is warranted. We evaluated the effects of OCA on multiparametric, MRI-derived, iron-corrected T1 (cT1) mapping, which is thought to correlate with hepatic fibroinflammatory disease and predict clinical outcomes.

Multiparametric MRI by LiverMultiScan (Perspectum Diagnostics, UK) was performed in a subset of REGENERATE NASH patients with fibrosis stage 2 or 3 (N=20) randomized 1:1:1 to placebo (n=7), OCA 10 mg (n=6), or OCA 25 mg (n=7). Changes in cT1and liver fat content were evaluated following 18 months of treatment.

At baseline, mean (SD) cT1 was similar in the placebo, OCA 10-mg, and OCA 25-mg groups (856.7 [106.8] ms; 943.2 [116.11] ms; and 882.1 [94.75] ms, respectively). Following 18 months of treatment, a dose-dependent reduction in mean cT1 from baseline was observed (placebo: -1.4 ms; OCA 10 mg: -59.6 ms; OCA 25 mg: -91.7 ms). At baseline, mean liver fat content was 16.29% (placebo), 19.27% (OCA 10 mg), and 15.3% (OCA 25 mg). Modest reduction (-7.9%) in fat content occurred in the OCA 25-mg arm at 6 months and was generally sustained through 18 months (figure 1).

Treatment with OCA resulted in dose-dependent improvements in cT1 and liver fat content measured noninvasively by multiparametric MRI, which may be consistent with histologic improvements and serum-based non-invasive markers of steatohepatitis and fibrosis.