The Impact of Obeticholic Acid on Atherogenic Lipoproteins in Nonalcoholic Steatohepatitis

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BACKGROUND

- Nonalcoholic fatty liver disease (NAFLD) is closely associated with cardiovascular disease (CVD) and CVD-related mortality
- An independent association between NAFLD and atherogenic dyslipidemia characterized by increased in VLDL, small dense LDL (sdLDL), and smaller LDL particle size has been reported
- Obeticholic acid (OCA), a FXR agonist, improves histological severity in NASH but increased LDL-cholesterol (LDL-C)
- The impact of OCA on atherogenic dyslipidemia in NAFLD is currently unknown

AIM

To determine the impact of OCA and histological response on lipoproteins in patients with NASH

METHODS

- FLINT trial was a multicenter, double-blinded, clinical trial that randomized non-cirrhotic patients with NASH to either placebo or OCA for 72 weeks.
- Samples from patients enrolled in FLINT trial in either the OCA arm (N=99) or placebo arm (N=97) on whom baseline, 12 weeks and end of treatment (EOT) biopsies were available were analyzed
- Lipoproteins analysis were performed using Nuclear Magnetic Resonance
- Histological response defined as 2+ reduction in NAS with no worsening of fibrosis

RESULTS

CONCLUSIONS

Obeticholic acid is associated with increase production of small VLDL particles. OCA use did not affect the more atherogenic lipoproteins including large VLDL particles or small dense LDL particles. Cessation of OCA resulted in restoration of lipoprotein abnormalities back to baseline

Summary of Key Findings

- In placebo arm, histological response was associated with greater mean change from baseline to 12 weeks in LDL-C (-15 vs. -3 mg/dL, P=0.04) and large LDL-P (-89 vs. 8 nmol/L, P=0.02)
- In OCA arm, histological response was associated with LDL-C change (17.4 vs. 34 mg/dL, P=0.02).
- None of the other lipoproteins changed significantly with resolution of NASH in either arm
- Statin use was similar across arms both at baseline and EOT and did not influence the results

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