IMPACT ON INFLAMMATORY BIOMARKERS, LIPIDS, AND CARDIOVASCULAR SAFETY OF CENICRIVIROC WITH OR WITHOUT STATINS IN SUBJECTS WITH NASH AND SIGNIFICANT LIVER FIBROSIS: CENTAUR STUDY

Kris V Kowdley, William Alazawi, Nicolas Lanthier, Alexandru Iacob, Richard Torstenson, Star Seyedkazemi, Gerardo Rodriguez-Araujo, Manal F. Abdelmalek, Arun J Sanyal

Washington State University,

University of London,

Cliniques Universitaires Saint-Luc,

AbbVie Inc., Madison, NJ,

AbbVie Inc., Stockholm,

AbbVie Inc., South San Francisco, CA,

AbbVie Inc., Irvine, CA, ,

Duke University,

Virginia Commonwealth University.

Background: Statins are commonly used to treat patients with dyslipidemia, a common comorbidity of nonalcoholic steatohepatitis (NASH) and advanced liver fibrosis. Cenicriviroc (CVC) is a potent C-C chemokine receptor types 2/5 inhibitor under development for liver fibrosis associated with NASH. CVC increases the exposure of some HMG-CoA reductase inhibitors and co-administration may require reduced dosing of these statins. This analysis assessed the impact of CVC and statin administration on inflammatory biomarkers, lipids, and cardiovascular (CV) safety in subjects with significant fibrosis from CENTAUR (NCT02217475).

Methods: Comparative analysis for lipid profiles, inflammatory biomarkers, and CV events was performed using data from modified intent-to-treat (mITT) subjects with biopsy-proven NASH and fibrosis stages F2 and F3 (NASH Clinical Research Network) grouped by placebo (pbo), CVC, statin, and CVC + statin treatment. Statin use was defined as uninterrupted use of atorvastatin 20 mg, fluvastatin 20 mg, pravastatin 20 mg, rosuvastatin 10 mg, or simvastatin 10 mg during the study. Groups were compared at Year 1 (Y1) using means and least square mean change from baseline (LSMcB). CV safety analysis at Y1 and Y2 were included.

Results: 166 mITT subjects were assessed in the 4 groups (n=51 [pbo]; 49 [CVC]; 33 [statin]; 33 [CVC + statin]). CVC + statin treatment reduced LDL, hs-CRP, and TNFα from baseline (Table). CVC decreased IL-6 and IL-1β. Target engagement markers CCL2/5 were similar with CVC treatment with or without statins. HDL, non-HDL, total cholesterol, and triglycerides were not significantly different for all treatment groups. CV adverse events (AEs) were not statistically different between groups for Y1/2.

Conclusion: CVC administered with or without statins had no negative effects on lipid profile or incidence of CV AEs in subjects with significant NASH-related liver fibrosis. Despite NASH patients expressing lower LDL receptors, modest reductions in LDL were observed with CVC and statin co-administration. Also, CVC plus statins reduced systemic inflammatory markers hs-CRP, TNFα, and IL-1β. Effect of CVC treatment on CV markers warrants further research in a larger cohort with longer exposure times. Editorial assistance by Complete HealthVizion.

	Placebo	CVC	Statin	CVC + statin
Baseline				
LDL, mean, mg/dL	131.95	123.22	100.92	109.48
hs-CRP, mean, mg/L	5.32	4.13	3.11	2.69
TNFα, mean, pg/mL	16.70	14.76	13.81	15.17
IL-6, mean, pg/mL	6.26	19.35	5.06	4.65
IL-1β, mean, pg/mL	0.07	0.21	0.06	0.22
Year 1				
LDL, mean (LSMcB), mg/dL	126.03 (−1.00)	124.71 (3.17)	101.42 (−6.11)	103.20 (−9.71)*
hs-CRP, mean (LSMcB), mg/L	6.47 (1.41)	5.44 (1.34)	3.85 (0.58)	1.76 (−1.17)
TNFα, mean (LSMcB), pg/mL	16.39 (0.23)	14.94 (0.01)	13.32 (−1.01)	13.58 (−1.62)**
IL-6, mean (LSMcB), pg/mL	4.88 (−1.10)	18.99 (−1.34)*	4.76 (0.09)	3.15 (−1.07)
IL-1β, mean (LSMcB), pg/mL	0.09 (−0.05)**	0.10 (−0.03)*	0.07 (−0.07)***	0.07 (−0.07)***

*p≤0.05; **p<0.01; ***p<0.001

CVC, cenicriviroc; hs-CRP, high-sensitivity C-reactive protein; IL, interleukin; LDL, low-density lipoprotein; LSMcB, least squares mean change from baseline; TNFα, tumor necrosis factor alpha