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Prevention

ETC-1002 LOWERS LDL-C AND BENEFICIALLY MODULATES OTHER CARDIO-METABOLIC RISK FACTORS IN HYPERCHOLESTEROLEMIC SUBJECTS WITH EITHER NORMAL OR ELEVATED TRIGLYCERIDES

ACC Oral Contributions

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Background: ETC-1002 improves imbalances in lipid and carbohydrate metabolism by activating AMP-kinase and affecting enzymes critical to fatty acid, cholesterol and glucose pathways. In this Phase 2, double-blind, parallel group, multi-center study, the lipid-regulating efficacy and safety of ETC-1002 were assessed.

Methods: After wash-out of their lipid-regulating drugs, 177 subjects with elevated LDL-C (130-220 mg/dL) were stratified by baseline triglycerides (TG; <150 or 150-399 mg/dL) and randomized to receive 40, 80 or 120 mg of ETC-1002 or placebo once daily for 12 weeks. The primary endpoint was percent change from baseline in LDL-C versus placebo both within and across TG strata.

Results: Treatment with ETC-1002 40 mg, 80 mg and 120 mg lowered LDL-C (least squares mean \pm SE) by $18\% \pm 2.2$, $25\% \pm 2.1$, and $27\% \pm 2.2$, respectively, versus a reduction of $2\% \pm 2.2$ by placebo ($p < 0.0001$ for each dose versus placebo). Other LDL parameters including ApoB, LDL particle number, and nonHDL-C were also lowered in a similar dose-dependent manner ($p < 0.0001$ for each dose versus placebo). Reductions in all LDL biomarkers were shown to be independent of baseline TG ($p < 0.05$ for each dose versus placebo within each TG stratum). Although mild decreases in TG and increases in HDL parameters were observed, these results were not consistently statistically significant or dose related. Post hoc analyses of subgroups with elevations in CRP (≥ 2 mg/L), blood pressure ($>120/80$ mmHg) and insulin (≥ 12 μ U/mL) were beneficially altered by treatment with ETC-1002. Adverse events and other safety assessments differed little between ETC-1002 and placebo groups.

Conclusions: ETC-1002 significantly lowered LDL-C up to 27% across a broad range of baseline TG levels and was generally safe and well-tolerated. There were beneficial changes in other cardio-metabolic risk factors.