Gemcabene Monotherapy and in Combination with Atorvastatin Lowers High Sensitivity C-Reactive Protein (hsCRP) in a Phase 2 Clinical Trial

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ABSTRACT

Background: Inflammation plays a key role in the progression of atherosclerosis, and serum high sensitivity c-reactive protein (hsCRP) has been recognized as a marker of cardiovascular risk. Lipid-lowering drugs such as statins also reduce hsCRP and may be more likely to reduce cardiovascular events than their lipid-lowering effects alone. Gemcabene is an inhibitor of hepatic cholesterol triglyceride and apoCIIII synthesis resulting in decreased assembly of VLDL and enhanced systemic clearance of VLDL. Gemcabene also reduces production of remnant particles, including LDL.

Methods: In this Phase 2 study, gemcabene 300, 600, and 900 mg/day was administered as monotherapy or in combination with atorvastatin 10, 40 and 80 mg/day in a randomized, placebo-controlled, double-blind, dose-ranging, efficacy and safety Phase 2 study, gemcabene 300, 600, and 900 mg/day was administered as monotherapy or in combination with atorvastatin 10, 40 and 80 mg/day in a randomized, placebo-controlled, double-blind, dose-ranging, efficacy and safety Phase 2 study.

Results: A secondary objective of this study was to evaluate the modulation of hsCRP by gemcabene. In 277 patients randomized, 250 (90%) completed the study. The baseline mean LDL-C was 174 mg/dL, and median hsCRP was 3.5 mg/L. Of the 277 patients, 165 (59.5%) were fasted when hsCRP was measured. The per-protocol analysis indicated that gemcabene demonstrated a lower hsCRP in patients with LDL-C <100 mg/dL, compared to patients with <150 mg/dL. Similar findings of reduced hsCRP were observed with losartan in the AIR Force/Texas Coronary Atherothrombosis Prevention Study (LIPID) randomized to LDL-C <130 mg/dL compared to patients with >190 mg/dL. Furthermore, patients during the trial who had both LDL-C <70 mg/dL and hsCRP <2 mg/L in a subgroup analysis of patients with hypercholesterolemic cardiovascular disease (CVD) events compared to patients with both LDL-C and hsCRP above these cut-points (2).

There is no correlation between lowering of LDL-C and lowering of hsCRP, as indicated by several categories of lipid-lowering therapies including statines, fibrates and the recently approved gemcabene.CONCLUSIONS: Gemcabene reduces hsCRP concentration in patients with hypercholesterolemic cardiovascular disease, and it has the potential to be used as a monotherapy or in combination with atorvastatin to achieve a significant reduction in hsCRP.

REFERENCES


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