Abstract: **P4606**

**Comparing biomarker profiles in patients with stable atherosclerosis treated with anacetrapib versus placebo: a nested proteomic study from HPS3/TIMI 55-REVEAL**

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**Topic(s):**
Coronary Artery Disease: Pharmacotherapy

**Citation:**

**Funding Acknowledgements:**
HPS3/TIMI 55-REVEAL was sponsored by Merck.

Background: The cholesteryl ester transfer protein (CETP) inhibitor anacetrapib improves cardiovascular outcomes in patients with stable atherosclerosis; however, the potential interaction of HDL-C-, LDL-C-, and non-lipid-mediated effects remains incompletely understood.

Purpose: The aim of this study was to identify biological pathways that are influenced by treatment with anacetrapib.

Methods: HPS3/TIMI 55-REVEAL was a randomized, double-blind, placebo-controlled trial of anacetrapib in patients with stable atherosclerotic cardiovascular disease. We performed a nested prospective biomarker study in 500 patients, analyzing 274 candidate biomarkers. We compared changes in biomarker levels between randomization and mid-study (~2 years) in patients treated with anacetrapib vs. placebo using a stringent threshold for statistical significance. We evaluated associations between changes in selected biomarkers and changes in HDL-C and LDL-C from baseline to mid-study in each treatment group.

Results: Eleven biomarkers were significantly modified by anacetrapib vs. placebo (Figure). These proteins represent pathways implicated in inflammation, lipid metabolism, and hematopoiesis. Among anacetrapib-treated patients, changes in 5/11 biomarkers were not significantly correlated with changes in either serum HDL-C or serum LDL-C.

Conclusion(s): In patients with stable atherosclerosis, treatment with anacetrapib results in changes in protein expression extending beyond lipid metabolism. Some of these changes appear to be independent of anacetrapib-mediated effects on HDL-C and LDL-C.
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