

What is Amarin's opinion on the REVEAL trial results on anacetrapib?

The REVEAL trial assessed the efficacy and safety of adding anacetrapib vs. placebo to effective doses of atorvastatin among patients with established occlusive vascular disease. The study achieved a 9% reduction in major coronary events and showed to double HDL-cholesterol. However, certain potential safety considerations, including accumulation in adipose tissue, have been raised regarding anacetrapib. In addition, failed prior clinical studies of other CTEP inhibitors and failed prior clinical studies of other therapies which increase HDL-cholesterol have resulted in continued questions regarding the appropriate role of this therapy. These concerns have elicited questions related to whether the drug will be advanced through the approval process and brought to commercialization.¹

The REVEAL trial and related analysis, while positive, appear to emphasize three important factors:

- 1) Significant residual cardiovascular risk remains for tens of millions of patients beyond the current standard of care for at-risk patients.
- 2) Improvement in select lipid parameters may not provide a complete picture on a drug's ability to affect cardiovascular risk reduction. For example, CTEP inhibitors such as anacetrapib improved certain lipid levels, but it has been discussed that very small lipid-poor LDL particles that are associated with angiographic progression of coronary heart disease may be preferentially elevated by anacetrapib treatment. The REVEAL results will undoubtedly be reviewed further, including via post-study follow up of patients, which may lead to better clarification regarding anacetrapib's mechanism of action and related effects.
- 3) Pragmatic treatment is important, including efficacy, safety, ease of use (tolerability), affordable cost and fitness for the treatment paradigm. Lowering cardiovascular risk alone is not necessarily sufficient to meet expectations of all healthcare providers and payers.

Amarin believes that residual risk beyond LDL lowering is essential to tackling cardiovascular disease. We welcome new therapies and clinical results to advance scientific understanding regarding how to best treat patients at high risk of cardiovascular disease. Amarin believes that if its REDUCE-IT trial is successful that Vascepa could be well positioned to potentially become pragmatic therapy for use in treating millions of patients who, despite the benefits of statin therapy, have persistent elevated triglyceride levels and remain at risk for cardiovascular disease.

¹ <https://www.nytimes.com/aponline/2017/08/29/health/ap-us-med-merck-cholesterol-drug.html?mcubz=0>