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Chronic CAD/Stable Ischemic Heart Disease

EFFECT OF MIPOMERSEN ON LIPOPROTEIN(A) IN PATIENTS WITH HYPERCHOLESTEROLEMIA ACROSS FOUR PHASE III STUDIES

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Background: Lipoprotein(a) [Lp(a)] is an independent, causal, genetic risk factor for cardiovascular disease (CVD). Elevated Lp(a) levels confer additional CVD risk to that predicted by LDL-C levels alone. Patients with Familial Hypercholesterolemia (FH) generally have a 2-fold increase in Lp(a) levels compared to non-FH patients. Current pharmacological lipid lowering therapies are ineffective in optimally treating elevated Lp(a) levels.

Methods: We evaluated the effect of mipomersen, an antisense apoB synthesis inhibitor, on Lp(a) levels in 4 Phase III studies in patients with FH or severe hypercholesterolemia at risk for CVD already receiving maximally tolerated lipid lowering therapy. Patients were randomized 2:1 to weekly subcutaneous injections of mipomersen 200 mg or placebo for 26 weeks. We present data in a subset of patients with a baseline Lp(a) >30 mg/dL, the threshold at which Lp(a) atherogenicity increases significantly.

Results: At baseline, 216 of the 391 randomized patients in the four studies had Lp(a) levels >30 mg/dL; 152 of these were treated with mipomersen. After 26 weeks of mipomersen treatment, the fraction of patients with baseline Lp(a) levels > 30 mg/dL that achieved Lp(a) levels ≤ 30 mg/dL ranged from 10 to 32% per study, with the greatest fractions in the homozygous FH (32%) and severe heterozygous FH (29%) studies. The median Lp(a) in mipomersen-treated patients was reduced from a range of 61 to 93 mg/dL across studies at baseline to 39.5 to 81 mg/dL after treatment. Significant reductions in mean apo B (26-36%) and LDL-C (24-35%) were also noted. Mipomersen treatment was associated with a safety profile consistent with that in earlier clinical trials. The most commonly reported adverse events were injection site reactions and flu-like symptoms.

Conclusions: Mipomersen is the first pharmacological therapy to consistently and effectively reduce Lp(a) levels in patients with FH or severe hypercholesterolemia and high CVD risk. Future studies need to confirm the role of Lp(a) as a modifiable risk factor in FH and CVD.