Efficacy and Safety of Combining Alirocumab With Atorvastatin or Rosuvastatin versus Statin Intensification or Adding Ezetimibe in High Cardiovascular Risk Patients: ODYSSEY OPTIONS I and II

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Background: ODYSSEY OPTIONS I and II (NCT01730040; NCT01730053) compared the efficacy and safety of alirocumab (ALI), a fully-human monoclonal PCSK9 antibody, as add-on to statin vs. doubling statin dose, switching to a more potent statin or adding ezetimibe (EZE) in patients (pts) not at goal on commonly used statin doses.

Methods: Patients (pts) had either prior CV disease (CVD) and LDL-C =70 mg/dL or CVD risk factors and LDL-C =100 mg/dL. Pts on stable atorvastatin (ATV) 20 or 40 mg/day (OPTIONS I) or rosuvastatin (RSV) 10 or 20 mg/day (OPTIONS II) were randomized to: (1) add-on ALI 75 mg every 2 weeks (Q2W); (2) add-on EZE 10 mg/day; (3) doubling of statin dose; or (4) switch from ATV 40 mg to RSV 40 mg (OPTIONS I only). ALI dose was increased at Week (W) 12 in a blinded manner to 150 mg Q2W if pts W8 LDL-C level was =70 or =100 mg/dL depending on CV risk (all doses self-administered subcutaneously via 1-mL pre-filled pen). Primary endpoints were the % change in LDL-C from baseline to W24 (intent-to-treat analysis). Safety data were pooled across statin entry regimens for each study.

Results: At W24, ALI significantly reduced LDL-C vs. all comparators in OPTIONS I and for pts entering on RSV 10 mg in OPTIONS II (p=0.0004; Table).

~79-92% ALI pts did not need dose increase (Table). In OPTIONS I, treatment-emergent adverse events (TEAEs) were reported by 65.4% ALI+ATV pts, 64.4% EZE+ATV pts, and 63.8% pts with doubling of ATV dose or switch to RSV. TEAEs in OPTIONS II were reported by 56.3% ALI+RSV pts, 53.5% EZE+RSV pts and 67.3% pts
with doubling of RSV dose. In both trials, the % of pts reporting SAEs ranged 3.8%-7.9% and TEAEs leading to discontinuation ranged 4.0%-7.9%; rates were comparable among groups. Most common TEAEs (both studies) were nasopharyngitis and URTI.

**Conclusions:** Adding ALI to ATV significantly reduced LDL-C more than adding EZE, doubling ATV dose or switching ATV 40 to RSV 40 mg, with similar results observed when adding ALI to RSV 10 mg. TEAEs were comparable between groups.

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