A 24-WEEK STUDY OF ALIROCUMAB AS MONOTHERAPY VERSUS EZETIMIBE: THE FIRST PHASE 3 DATA OF A PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 9 INHIBITOR

Poster Contributions
Hall C
Sunday, March 30, 2014, 9:45 a.m.-10:30 a.m.

Session Title: Prevention: Familial Hypercholesterolemia, Novel Therapies and Cardiovascular Risk
Abstract Category: 20. Prevention: Clinical
Presentation Number: 1183-125

Authors: Eli M. Roth, Marja-Riitta Taskinen, Henry Ginsberg, John Kastelein, Helen M. Colhoun, Laurence Merlet, Robert Pordy, Marie T. Baccara-Dinet, Sanofi, Paris, France, Regeneron, Tarrytown, NY, USA

Background: Alirocumab is a fully human monoclonal antibody to proprotein convertase subtilisin/kexin type 9 (PCSK9). The aim of this 24-week trial (NCT01644474; ODYSSEY MONO) was to compare the low-density lipoprotein cholesterol (LDL-C)-lowering efficacy and safety of alirocumab versus ezetimibe (EZE) over 24 weeks in patients with hypercholesterolemia, not receiving statin or other lipid-lowering therapies.

Methods: This was a Phase 3, randomized, double-blind, double-dummy study in patients with LDL-C 100-190 mg/dL and estimated 10-year fatal cardiovascular disease risk SCORE ≥ 1% and < 5%. Patients received EZE 10 mg daily (n=51) or alirocumab 75 mg subcutaneously every 2 weeks (Q2W) (n=52), with the dose up-titrated in a blinded manner to 150 mg Q2W at Week 12 if Week 8 LDL-C ≥ 70 mg/dL. Alirocumab and the alirocumab placebo in the EZE arm were self-administered as single, 1-mL, subcutaneous injections via autoinjector. Primary endpoint was mean % change in LDL-C from baseline to 24 weeks, analyzed using a mixed-effect model with repeated measures approach (intent-to-treat population). All post-baseline data available from Weeks 4 to 24 were used. Adverse events (AEs) and clinical laboratory values were also assessed.

Results: Mean (SD) baseline LDL-C levels were 141.1 (27.1) mg/dL in the alirocumab arm and 138.3 (24.5) mg/dL in the EZE arm. Overall, 44/52 (84.6%) and 44/51 (86.3%) patients in the alirocumab and EZE arms, respectively, completed the 24-weeks treatment period. 14 patients in the alirocumab arm were up-titrated at Week 12 to 150 mg Q2W. Least-squares mean (SE) LDL-C reduction from baseline to Week 24 was 47.2 (±3.0) % with alirocumab versus 15.6 (+3.1) % with EZE (P<0.0001). Treatment emergent AEs occurred in 69.2% and 78.4% of alirocumab and EZE patients, respectively. Injection-site reactions were infrequent (< 4% of patients in both groups). Muscle-related AEs occurred in 3.8% of alirocumab and 3.9% of EZE patients.

Conclusions: This first Phase 3 trial of a PCSK9 inhibitor, alirocumab, demonstrated significantly greater LDL-C lowering with alirocumab compared to EZE after 24 weeks of treatment. AEs were comparable between groups and injection site reactions were infrequent.