Impact of chronic kidney disease on mid-term prognosis of stable angina patients with high-dose or low-dose pitavastatin treatment: REAL-CAD sub-study

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On behalf of REAL-CAD study

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Background: We previously demonstrated that high-dose (4 mg/day) compared with low-dose (1 mg/day) pitavastatin therapy significantly reduced cardiovascular events in Japanese patients with stable coronary artery disease in the Randomized Evaluation of Aggressive or Moderate Lipid Lowering Therapy with Pitavastatin in Coronary Artery Disease (REAL-CAD) study. However, little is known about whether the advantage of high-dose statins over low-dose statins is consistent among non-, mild, and moderate to severe chronic kidney disease (CKD) patients.

Purpose: The aim of this study was to clarify the effect of high-dose statins on cardiovascular events in Japanese patients with or without CKD.

Methods: The REAL-CAD study is a prospective, multicenter, randomized, open-label, blinded endpoint, physician-initiated superiority trial. In this sub-analysis of REAL-CAD study, patients were categorized into three groups according to estimated glomerular filtration rate (eGFR). Patients on hemodialysis were excluded in this study. The primary endpoint was a composite of cardiovascular death, non-fatal myocardial infarction (MI), non-fatal ischemic stroke, or unstable angina requiring emergency hospitalization. A secondary composite endpoint was defined as a composite of the primary endpoint event or clinically-indicated coronary revascularization excluding target-lesion revascularization.

Results: The total population of the REAL-CAD study was 12,413 patients. After exclusion of patients lacking eGFR data, the numbers of patients categorized into non-CKD (eGFR $\geq$60 mL/min/1.73m^2), mild CKD (eGFR; 45–60), and moderate to severe CKD (eGFR $<$45) were 7,778 (64%), 3,176 (26%), and 1,164 (10%), respectively. The median follow-up period was 3.9 years. The baseline characteristics and medications were well balanced between the two groups in each CKD group. While high-dose compared to low-dose pitavastatin significantly reduced the primary endpoint in non-CKD patients, the effect was not observed in mild CKD and moderate to severe CKD patients (Figure 1). High-dose compared with low-dose pitavastatin did not significantly reduce the secondary composite endpoint in both mild and moderate to severe CKD patients as well. High-dose pitavastatin significantly reduced the risks of MI and any coronary revascularization in non-CKD patients, however, the effects were diminished in mild CKD and moderate to severe CKD patients. There was no significant difference between high-dose and low-dose pitavastatin treatment in the risk of all-cause death, cardiovascular death, ischemic stroke, or unstable angina requiring emergency hospitalization in patients with or without CKD.

Conclusion: Although high-dose pitavastatin therapy significantly reduced cardiovascular events in non-CKD patients with stable angina compared to low-dose pitavastatin, such beneficial effects had diminished in Japanese patients with mild or moderate to severe CKD patients.

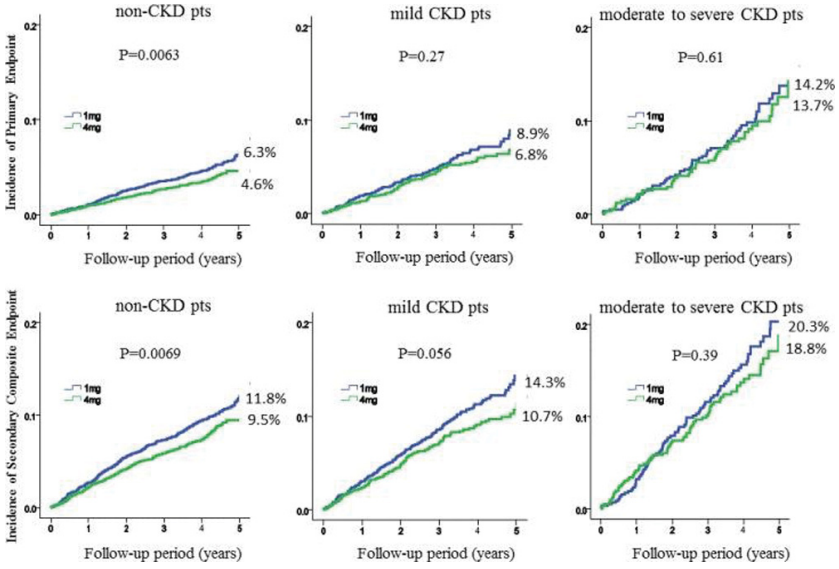

Figure 1. Kaplan-Meier Curves for Endpoints