The Influence of OATP1B1 and BCRP Genotypes on the Lipid Lowering Effect after Administration of Rosuvastatin in Hyperlipidemia Patients
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Purpose
Rosuvastatin, a HMG-CoA reductase inhibitor, is used to prevent cardiovascular disease by lowering the concentration of blood low-density lipoprotein cholesterol (LDL-C). Rosuvastatin enters the liver by organic anion-transporting peptide (OATP)1B1 and excreted to bile by breast cancer resistance protein (BCRP). This study identified the influence of OATP1B1 (SLCO1B1*15 or *17) and BCRP (ABCG2 421C>A) genotypes on pharmacokinetics, lipid lowering effect and safety of rosuvastatin in hyperlipidemia patients.

Methods
A total of 17 subjects with LDL cholesterol level more than 130 mg/dL received rosuvastatin 20 mg once daily for 8 weeks. Blood samples for pharmacokinetic and lipid lowering effect analysis was collected on Day 1, 15, 29, 43, and 57 and the blood sampling was conducted before dosing except on Day 57. Plasma concentration was analyzed by chromatography-tandem mass spectrometry (LC-MS/MS). Safety profiles were evaluated by monitoring adverse events (AEs) and clinical evaluations.

Results
Subjects were divided by 3 genotype groups, wild type (SLCO1B1 *1/*1, ABCG2 CC), OATP1B1 variant (SLCO1B1 *1/*15, *1/*17, or *17/*17, ABCG2 CA or AA), and BCRP variant (SLCO1B1 *1/*1, ABCG2 CA or AA). OATP1B1 variant and BCRP variant showed higher trough concentration of rosuvastatin by 3.1-5.3 folds and 1.4-2.0 folds, respectively, when compared to the wild type group. The lipid lowering effect was evaluated by the concentrations of LDL-C, total cholesterol, triglyceride, and high-density lipoprotein cholesterol (HDL-C) and the decrease of HDL on Day 15 (P=0.046), total cholesterol and LDL on Day 29 (P=0.042 and P=0.025, respectively) and Day 57 (P=0.018 and P=0.018, respectively) from the baseline was significantly different between genotype groups. BCRP variant showed the highest decrease from the baseline. All of the AEs were mild and there were no significant differences of the number of AEs between genotype groups.

Conclusion
Rosuvastatin was generally well tolerated in hyperlipidemia patients and the genetic variants of OATP1B1 and BCRP influenced on the pharmacokinetics and lipid lowering effect of rosuvastatin.