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ABCG2 Polymorphism Markedly Affects the Pharmacokinetics of Atorvastatin and Rosuvastatin

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The ABCG2 c.421C>A single-nucleotide polymorphism (SNP) was determined in 660 healthy Finnish volunteers, of whom 32 participated in a pharmacokinetic crossover study involving the administration of 20 mg atorvastatin and rosuvastatin. The frequency of the c.421A variant allele was 9.5% (95% confidence interval 8.1–11.3%). Subjects with the c.421AA genotype (n = 4) had a 72% larger mean area under the plasma atorvastatin concentration–time curve from time 0 to infinity ($AUC_{0-\infty}$) than individuals with the c.421CC genotype had (n = 16; P = 0.049). In participants with the c.421AA genotype, the rosuvastatin $AUC_{0-\infty}$ was 100% greater than in those with c.421CA (n = 12) and 144% greater than in those with the c.421CC genotype. Also, those with the c.421AA genotype showed peak

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plasma rosuvastatin concentrations 108% higher than those in the c.421CA genotype group and 131% higher than those in the c.421CC genotype group ($P \leq 0.01$). In MDCKII-ABCG2 cells, atorvastatin transport was increased in the apical direction as compared with vector control cells (transport ratio 1.9 ± 0.1 vs. 1.1 ± 0.1). These results indicate that the ABCG2 polymorphism markedly affects the pharmacokinetics of atorvastatin and, even more so, of rosuvastatin—potentially affecting the efficacy and toxicity of statin therapy.

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