# Effects of ABCB1 and ABCG2 polymorphisms on the pharmacokinetics of abemaciclib

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September 24, 2021

## Abstract

Aim: The adverse events of the CKD4/6 inhibitor abemaciclib are known to be dose dependent. However, its pharmacokinetics vary among individuals. Abemaciclib is reported to be transported by P-glycoprotein (P-gp) and the breast cancer resistance protein (BCRP). Therefore, we evaluated whether ABCB1 and ABCG2 gene polymorphisms could be pharmacokinetic predictive factors of abemaciclib. Methods: A total of 45 patients with breast cancer able to take abemaciclib (150 mg twice daily) for 2 weeks were evaluated to determine the association among abemaciclib concentrations, adverse events, and ABCB1 1236T>C, 2677G>T/A, 3435C>T, and ABCG2 421C>A gene polymorphisms. Results: The trough concentrations of abemaciclib were higher in the group with grade 2 or greater neutropenia, anemia, and thrombocytopenia as compared with the group with grades 0 or 1. No significant association was observed between ABCB1 1236T>C, 3435C>T, and ABCG2 421C>A gene polymorphisms and abemaciclib concentrations. However, in ABCB1 2677G>T/A polymorphisms, the concentrations of abemaciclib tended to be higher in the homozygous group (AA + AT) as compared with that in the wild-type and heterozygous group (GG + GA + GT) [222.8 (80.5–295.8) ng/mL vs. 115.8 (23.6–355.2) ng/mL, P = 0.11]. Hence, the ABCB1 2677G>T/A homozygous group had a significantly higher incidence of abemaciclib withdrawal and dose reduction within 4 weeks as compared than the wild-type and heterozygous group (67% vs. 33%, P = 0.03). Conclusions: The gene polymorphism of ABCB1 2677G> T/A might be a predictor of the pharmacokinetics and tolerability of abemaciclib.

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