UGT1A1*6 polymorphisms are predictive of high plasma concentrations of dolutegravir in Japanese individuals

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Background Dolutegravir (DTG), an HIV integrase inhibitor, is metabolised mainly by glucuronidation via UDP-glucuronosyltransferase 1A1 (UGT1A1). Several UGT1A1 polymorphisms have been correlated with UGT1A1 expression level or enzymatic activity. We compared the effect of two polymorphic alleles in this gene, UGT1A1*6 and UGT1A1*28, on plasma DTG concentrations in Japanese HIV-infected patients.

Methods The plasma trough DTG concentration was measured in 69 HIV-1 patients taking DTG at Osaka National Hospital, and UGT1A1 genetic screening (*6 and *28) was performed. UGT1A1 was genotyped using the sequence method. Plasma was sampled immediately before taking DTG, and plasma DTG concentrations were determined using a liquid chromatography-mass-spectrometry method.

Results In the 69 patients who received DTG, the frequencies of UGT1A1*6 and UGT1A1*28 were 23% and 13%, respectively. The plasma trough concentrations of DTG in patients homozygous for UGT1A1*6 (n = 7, median: 1.4 µg/mL) were significantly higher than those in the patients carrying the normal allele (n = 32, median: 0.89 µg/mL; p = 0.011). The plasma trough concentrations of DTG in patients homozygous for UGT1A1*28 (n = 3, median: 1.2 µg/mL), compound heterozygous for UGT1A1*6 and UGT1A1*28 (n = 2, 0.98 and 1.2 µg/mL, respectively), and heterozygous for UGT1A1*6 and UGT1A1*28 (n = 15 and 10, median: 1.1 and 1.0 µg/mL, respectively) were not significantly different from those in the patients homozygous for the normal allele.

Conclusion The plasma trough concentration of DTG was significantly higher in patients who were homozygous for UGT1A1*6 than in those with the normal allele. This finding suggests that the presence of UGT1A1*6 influences the plasma DTG concentration.

Disclosure of interest statement Nothing to declare.