Correlation between UGT1A1*6 and *28 genotype, and plasma dolutegravir concentrations in Japanese HIV-1 infected patients

Hiroaki Togami¹, H. Yagura², A. Hirano³, M. Takahashi⁴, M. Yoshino⁴, K. Abe⁴, Y. Oishi⁴, S. Takematsu⁴, S. Kakigoshi⁵, Y. Yamamoto⁶, T. Ito⁷, M. Yamamoto⁶, Y. Mizumori⁸, O. Kanei¹, M. Usumi⁹, D. Watanabe⁵, Y. Yokomaku¹, T. Shirasaka²

¹National Hospital Organization Nagoya Medical Center, ²National Hospital Organization Osaka Medical Center, ³National Hospital Organization Suzuka Hospital, ⁴National Hospital Organization Osaka Minami Medical Center, ⁵National Hospital Organization Sendai Medical Center, ⁶National Hospital Organization Kyushu Medical Center, ⁷National Hospital Organization Kyoto Medical Center, ⁸National Hospital Organization Higashinagoya Hospital, ⁹National Hospital Organization Himeji Medical Center

Methods

We recruited 202 Japanese HIV-1 infected patients (male:female=191:11) in the National Hospital Organization, Japan. Next, we measured DTG plasma trough concentrations using LC-MS¹. We performed UGT1A1 genetic screening (*6 and *28). This study was reviewed and approved by the Institutional Review Board of the National Hospital Organization, and each subject provided written informed consent.

Results

- The trough concentrations of plasma DTG were significantly higher in patients homozygous for UGT1A1*6 (n=13, median: 1.82 µg/mL; p=0.001) than in patients carrying the normal allele (n=95, median: 0.82 µg/mL).
- The trough concentrations of DTG in patients homozygous for UGT1A1*6 (n=4, median: 0.92 µg/mL; p=0.001), heterozygous for UGT1A1*6 and *28 (n=45, median: 0.98; p=0.621), and compound heterozygous for UGT1A1*6/*28 (n=7, median: 1.18 µg/mL; p=0.189) were not significantly different from those in patients homozygous for the normal allele.

Conclusions

There were significant correlations between *6 allele and the plasma DTG concentrations. Therefore, UGT1A1*6 polymorphisms are predictive of high plasma concentrations of DTG in Asian patients. To prevent side effects of DTG, it is important to analyze UGT1A1*6 genotypes for Asian each patient.

References