EXECUTIVE SUMMARY FOR MSS 191 R
The implications of CYP2B6 genotype in long term efavirenz treatment

Aim and objectives. Highly active antiretroviral therapy (HAART) is the standard form of treatment for people living with human immunodeficiency virus (HIV) infection. Efavirenz (EFV), a non-nucleoside reverse transcriptase inhibitor, is a commonly used component of treatment regimens. Neurological side effects of EFV have been reported the occurrence of which was associated with the genetic polymorphism of hepatic cytochrome P450 (CYP) 2B6, its main metabolizing enzyme. With the aim of supporting the optimization of HAART, a study was conducted with the objectives of determining the plasma EFV level of patients on EFV-based regimens and following prolonged therapy, and assessing their associations with host CYP2B6-516 genotype.

Project design. Archived blood samples of EFV-treated patients attending the service of HIV specialist clinics in Hong Kong and who have been tested for plasma EFV levels under the Therapeutic Drug Monitoring (TDM) programme were accessed and evaluated. Their corresponding CYP2B6-516 genotypes were determined by real time PCR. Plasma levels of patients who have been tested more than once over time were examined for temporal changes.

Target population. People living with HIV

Main achievements. In this study, analyses were made on 95 patients on EFV-containing HAART regimens who had plasma EFV levels available, alongside their corresponding CYP2B6-516 genotype. The mean plasma level at baseline (between 2 months and 2 years) differed between genotypes: 2.89 ± 1.26 mg/L for GG, 3.65 ± 1.26mg/L for GT and 8.78 ± 2.66mg/L for TT. As a sub-study, 62 patients with GG or GT genotype who had plasma EFV levels at more than one time-point were evaluated. Comparison between GG and GT genotype in the fourth year did not show any statistically significant difference.

Conclusions. Whereas CYP2B6-516 TT genotype is associated with a 2-3 folds higher level of EFV, the difference between GG and GT is much smaller albeit of statistical significance. Over an interval of 4 or more years, this difference is no longer seen. This may be partly explained by the phenomenon of auto-induction after prolonged use of EFV.

PUBLICATIONS.
Under preparation