Retrovirology

Poster presentation

Detection of low frequency drug resistant mutations in antiretroviral-treated HIV-1C infections

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Purpose of the Study

The objective of this study is to identify low frequency mutations in HIV-1C that cannot be detected by standard genotyping. We analysed samples from the Tshepo cohort in Botswana. Tshepo is an open-label, unblinded, randomised 3 × 2 × 2 factorial design study comparing 1) the rate of development and specific types of drug resistance mutational patterns among HIV-1C-infected adults treated with 6 initial HAART regimens; (2) the tolerability and efficacy of these HAART regimens; (3) evaluation of the When to Start HAART question as patients are initiated on HAART in two different baseline CD4+ cell count strata; and (4) comparing the short- and long-term effectiveness of two operational adherence strategies.

Methods

Methodology involved quantification of the proviral load and multiple PCR with a single copy as a template followed by direct sequencing. Bulk sequencing was also carried out for each patient per time point.

Summary of Results

Of the patients who had been enrolled in the study for at least one year, had longitudinal samples at every two month visit and had failed the first-line therapy, failed therapy, 30% of them showed no drug resistance mutations prior to the point of virological failureby single genome sequencing. Single genome sequencing revealed drug resistance mutations for the remaining 70% of the patients before virological failure was experienced.

Conclusion

Single genome sequencing allows for the detection of low frequency mutation below the threshold of 30% for bulk sequencing, allows early detection of these mutations for some samples and in addition can detect mutations otherwise missed by conventional methods of detection