

Oral presentation

## O113 HIV-1 clade C resistance genotypes after first virological failure in a large community ART programme

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### Background

In sub-Saharan Africa large numbers of clade C HIV-infected individuals are exposed to antiretrovirals through prevention of mother-to-child transmission and through first-line non-nucleoside reverse transcriptase inhibitor-based (NNRTI) regimens. HIV drug resistance pre-treatment, as well as in those failing first-line ART, has not been adequately catalogued. Choice of second-line therapy would ideally be based on patterns of resistance at first-line failure.

### Methods

Genotypic resistance testing was performed on plasma samples from both treatment-naïve individuals and those failing first-line ART (confirmed HIV-RNA >1000 copies/ml) from public sector clinics in the Greater Cape Town area (2002–2007). We compared genotypic resistance profiles for ART-naïve patients and those who have failed ART. We examined whether time of genotyping was associated with differential distribution of resistance mutations.

### Summary of results

Samples from 230 patients (120 naïve; 110 with virologic failure) were included. 98% had clade C virus. Among naïve patients, prevalence of primary resistance was estimated at 2.5% (95% CI: 0.0%–5.3%). Three ART-naïve patients each had one important RT mutation: K65R, Y181C, G190A. Among NNRTI-treatment experienced patients, the estimated prevalence of resistance mutations was high. Ninety-six individuals (83%) had therapy-lim-

iting NNRTI mutations, including K103N (53%), V106M (31%), Y181C (9.4%). Eighty-one individuals (70%) had ≤2 NNRTI mutations; 15 (13%) had >3 NNRTI mutations. The M184V mutation was the most common single mutation in 91 patients (78%). Eleven of the patients with virologic breakthrough (9.5%) had the K65R mutation. A non-significant trend toward more individuals developing thymidine analogue mutations was noted when genotype was completed after 6 months on failing therapy [10/31 patients (32%)], compared to those who had genotyping before 6 months [16/79 patients (20%)].

### Conclusion

Prevalence of primary resistance in a sample of ART-naïve clade C HIV-infected individuals in South Africa is low. An NNRTI-based initial ART regimen remains appropriate for most naïve individuals. Patients failing first-line ART have generally developed resistance to both NNRTIs and NRTIs, the two drug classes used in first-line therapy. The emergence of the K65R mutation, without tenofovir use, is unexpected and worrisome. Current second-line ART options remain viable, but close ongoing surveillance of resistance patterns is critical to optimize clinical care.