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Oral presentation



# O124 Efavirenz and rifampicin in the South African context: is there a need to dose increase efavirenz with concurrent rifampicin therapy?

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## Background

In the developing world many people are co-infected with HIV and tuberculosis (TB). Recommended first-line antiretroviral therapy (ART) commonly includes efavirenz (EFV). Anti-tuberculous therapy includes rifampicin (RFN). There remains debate about whether a dose increase of EFV from the standard dose of 600 mg to an increased dose of 800 mg daily is required with concomitant RFN, which induces cytochrome p450 isoenzymes that may reduce levels of EFV.

## Methods

Individuals from the CIPRA-South Africa adult treatment cohort on EFV-based ART with concomitant TB were dosed with either an increased (800 mg) or standard (600 mg) dose of EFV during TB treatment. After TB therapy all were given standard EFV doses. Two mid-dose EFV concentrations were determined from each individual: the first after 4 weeks of concomitant EFV and RFN therapy, and the second at least 4 weeks after TB therapy was completed. Mid-dose EFV concentrations were compared across groups using the Mann-Whitney U-test and within individuals using the Wilcoxon signed rank test.

## Summary of results

Paired samples were collected from 60 individuals; 38 (63%) were women. The median weight was 60 kg (IQR 52–65 kg). The median CD4 count at ART baseline was 110 cells/mm3 (IQR 35–158), and median viral load 5.5 log (IQR 5.1–5.9). Thirty-one (52%) were taking 800 mg EFV during TB treatment and 29 (48%) had the standard dose. There was no significant difference in the median EFV concentrations on RFN in the 800 mg group [3.2 ug/ml (IQR 1.5–6.5)], compared to the 600 mg group [2.85 ug/ml (IQR 1.8–5.0)]. The median EFV concentrations off RFN did not differ significantly either [800 mg group: 2.15 ug/ml (IQR 1.38–3.09); 600 mg group: 2.4 ug/ml (IQR 1.4 to 4.3)]. There was no evidence of a difference between concentrations within the individual if on 600 mg dose at both timepoints nor if on 800 mg dose at first time-point. There was no increase in EFV-linked adverse effects in any group.

## Conclusion

In our population there is no reduction in mid-dose EFV concentrations with concomitant RFN therapy. The pharmacogenetic profile cytochrome p450 isoenzyme, particularly the 2B6 isoenzyme, in this South African population may differ from the other populations where the majority of pharmacokinetic work has been completed. It was not necessary to increase the dose of EFV during concomitant TB therapy in this South African population.