Comparing the effectiveness of Efavirenz and Nevirapine as first line antiretroviral treatment amongst a cohort of treatment naïve adult patients from South Africa

Peter Bock1,2, Geoffrey Fatti 1 & Ashraf Grimwood1

Affiliations: 1- Kheth’ Impilo, 2- PHC directorate. University of Cape Town

Background
There is an ongoing debate about the use of Efavirenz (EFV) and Nevirapine (NVP) for first line antiretroviral treatment (ART) in developing countries; fuelled by EFV’s link with teratogenicity in rats, NVP’s interactions with Rifampicin and the increased rates of virological failure amongst women exposed to single dose NVP during pregnancy. This paper compares the effectiveness of EFV and NVP in a multicentre adult cohort of ART patients attending public health facilities in South Africa.

Methods
A retrospective cohort analysis of routine data on 27350 ART naïve adults initiated between January 2004 and December 2007 at 56 public health sites across 4 provinces was completed. The primary outcomes were viral load suppression at 6 months and death; secondary outcomes included missing 6 months viral load results and change of ART regimen. Stata 9 was used to conduct analyses which included simple statistics, logistic regression and Cox proportional hazard models.

Results
Median follow up time was 9.3 (IQR: 4.6-17.7) months, median age was 34.3 (IQR: 29.4-40.8) years and the median baseline CD4 count 113 cells/mL (IQR= 57-165). Multivariate analyses showed patients receiving first line regimens containing EFV were more likely to achieve viral load suppression at 6 months (OR=1.24; 95%CI: 1.07-1.45) and less likely to change regimen (OR=0.53; 95%CI: 0.48-0.59). A subset analysis of 18527 patients, with baseline pregnancy status reported, showed no difference in hazard rates for death between the two groups (AHR=1.17; 95%CI: 0.99-1.37).

Discussion
These analyses concur with findings from other studies that have shown greater efficacy in viral load suppression amongst patients started on regimens with EFV when compared to NVP. Baseline analyses showed a greater occurrence of factors independently associated with increased death rates in the EFV cohort. In a further subset analyses of patients with baseline pregnancy status recorded, however, there was no difference in death rates. There were greater numbers of missing tests amongst male patients and patients managed at district and regional hospitals when compared to PHC clinics, as well as differences between provinces. Interprovincial differences are likely to be multifactorial, are difficult to interpret accurately and should be the subject of focussed research; however poorer outcomes in more rural provinces e.g. the Eastern Cape are consistent with previous publications.

These analyses also confirm the association between virological failure and death emphasising the usefulness of viral load measurements for clinical management. The high rates of missing viral load results reported here serves as a reminder of the potential for waste of scarce resources in large programmes in developing countries and strengthen the argument for introducing technology for point of care viral load and CD4 monitoring.

Conclusions
This data shows mixed results for patients on EFV with respect to measured outcomes and highlights some of the problems with commonly used non-nucleoside reverse transcriptase inhibitors (NNRTIs). Protease inhibitors are an effective alternative to NNRTIs; but are currently too costly for first line use in developing countries. There is an urgent need for further research into available NNRTIs and the distribution of suitable affordable alternatives. In the interim, the developing world needs to improve access to existing drugs and simultaneously implement more efficient strategies to help meet the ever increasing treatment need.

Acknowledgements
The authors would like to acknowledge the staff working at these clinics for all their hard work in improving the health of patients with HIV. In addition they would like to thank colleagues at Kheth’ Impilo who have assisted with the implementation of these programmes and the collection and processing of the data as well as Dr Nandi Siegfried from the MRC in Cape Town for her input and guidance on writing up the results.

Website: www.khethimpilo.org, Contact: Peter.Bock@khethimpilo.org