

**MAKERERE**



**UNIVERSITY**

**NON-LINEAR MIXED EFFECTS MODELING OF LIVER FUNCTION  
BIOMARKERS IN TB-HIV PATIENTS CO-TREATED WITH RIFAMPICIN  
AND EFAVIRENZ BASED REGIMENS**

BY

**BISASO KUTEESA RONALD, BPHARM (MAK)**

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# **ABSTRACT**

## **Introduction**

Survival has improved as a result of improved HIV therapy but liver disease remains a critical problem in HIV patients. HIV disease, ART and Tuberculosis treatments have all been documented to cause liver damage, but no published study on the ultimate subclinical effect of treatment on the liver.

## **Objectives**

To develop a mechanistic PK/PD model to characterize liver functional changes in HIV patients on EFV based HAART with or without TB treatment.

## **Materials and Methods**

CYP2B6\*6 & 11, CYP3A5 and ABCB1 genotypes, baseline age and weight, plasma Efavirenz, Creatinine, Albumin and ALT data were collected at specified times for 3 months from 262 HIV patients on EFV based HAART, of which 158 were on Rifampicin based anti-TB treatment for TB co-infection. A semi-mechanistic model based describing changes in plasma albumin concentration during treatment with HAART was developed and fit to the data using the laplacian method in NONMEM software version 7.2 and covariate analysis was done.

## **Results and conclusions**

The model had three fixed and two random effects parameters. It had a mean prediction error of 0.97% and precision of 87.13%. TB disease status and ABCB1c.3435C>T genotype were significant covariates ( $p < 0.01$ ). Albumin secretion rate in HIV patients was 39% lower at the start of HAART treatment and predicted to improve to approximately 84% of that reported in normal people over a 3 month treatment period. TB co-infection worsens the liver dysfunction caused by HIV. ABCB1c.3435C>T genotype is a predictor of the level of improvement in the rate of secretion of Albumin by the liver during treatment with HAART.