Shingirai Melidith Chiwambutsa

PhD candidate fellow in the Network for Oncology Research in Subsaharan Africa

University of the Witwatersrand, Johannesburg, South Africa

Pharmacokinetic and Pharmacogenetics modelling and simulation of tamoxifen in African women with breast cancer to guide individualized treatment

I aim at evaluating the effect of genetic polymorphism of tamoxifen metabolizing enzymes (CYP2D6, CYP3A4, CYP3A5, CYP2C9, CYP2C19 and CYP2B6) and co-medications in determining exposure levels of endoxifen in African descent breast cancer patients adhering to tamoxifen treatment and to develop an African population tamoxifen pharmacokinetic and pharmacogenetic model for the prediction of endoxifen exposure levels.

I will use secondary data collected for the HIV/ART and tamoxifen metabolism in black breast cancer patients in South Africa study, which is a sub-study of the South Africa Breast Cancer Health Outcomes Study (SABCHO). Descriptive statistical methods will be used to evaluate the effects of drug-gene and drug-drug interaction on tamoxifen efficacy. A Non Linear Mixed Effects (NLME) pharmacokinetic model (PK) for endoxifen and tamoxifen with first order absorption and elimination will be developed.

The results of this study will improve our understanding of the effects of genetic polymorphisms on tamoxifen metabolism and inter individual variations in the concentrations of tamoxifen metabolites. Moreover, the PK model will be used as a guide for personalised tamoxifen treatment and improve treatment outcomes in breast cancer women of African ancestry.

Research Task 4

Supervisors:
Prof. Collen Masimirembwa and Prof. Paul Ruff