Pharmacogenetics and Pharmacokinetics of Tamoxifen in a Zimbabwean breast cancer cohort

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Abstract

Tamoxifen is the most used hormonal therapy for estrogen receptor positive breast cancer. CYP2D6 is the main enzyme in the metabolic pathway of tamoxifen to endoxifen. Variations in endoxifen plasma concentrations are associated with CYP2D6 polymorphisms. This study aimed to determine the association between the CYP2D6 polymorphisms and endoxifen plasma concentrations in a cohort of Zimbabwean breast cancer patients (n = 40). TaqMan genotyping and copy number assays were done to determine CYP2D6 genotypes. Tamoxifen and metabolites were quantitated using LC-MS/MS. The population had high frequencies of the CYP2D6 reduced function alleles, *17 (15%) and *29 (18%). The median endoxifen concentration was 4.78 ng/ml and 55% of the patients, mostly intermediate metabolizers were below the endoxifen therapeutic threshold 5.97 ng/ml. The CYP2D6 phenotypes and activity scores were significantly associated with endoxifen plasma concentrations (p = 0.0151) and with endoxifen to N-desmethyl tamoxifen ratios (p = 0.0006).

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