

# “Evaluation of the Evolution in Relation to CYP2D6\*4 in Patients with Breast Cancer and Tamoxifen Users of Two Breast Services of Belo Horizonte.”



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## INTRODUCTION

Breast cancer (BC) is the malignancy with the highest incidence among women and with high mortality rates. Treatment is multidisciplinary, with the use of tamoxifen (TAM) one of the major therapeutic modalities. It is metabolized by the CYP2D6 enzyme in its active metabolites, 4-hydroxytamoxifen (HTF) and endoxifen (EDF), which are up to 100 times more potent than TAM in suppressing the proliferation of estrogen-dependent tumor cells. The reduction of the CYP2D6 activity is related to reduced levels of EDF and worse prognosis in women treated with TAM. This study aimed to evaluate the association of the polymorphism of CYP2D6\*4 and the evolution of patients with BC.

## METHODOLOGY

Interview with 138 patients with BC treated with TAM was performed. Clinical data and blood samples for genotyping of CYP2D6\*4 was collected from two Breast Services of Belo Horizonte. Patients were classified in relation to the polymorphism as extensive metabolizers (EM), intermediate metabolizers (IM) and poor metabolizers (PM). Statistically analyzed was performed from the result of polymorphism, the clinical characteristics of the patients, the tumor characteristics and evolutionary data, such as recurrence and survival.

## RESULTS

We observed that 14.5% of patients had recurrence (Figure 01) and 30% of premenopausal patients had menstrual cycles (Figure 02). The mean duration of disease-free survival (SVLD) in months was  $43.6 \pm 45.7$ , and the mean overall survival (OS) in months was  $44.5 \pm 46.1$ .

Figure 01: Recurrence

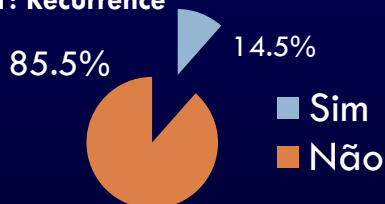


Figure 02: Menstrual Cycles



Regarding survival considering polymorphism, the patients who were EM had a higher survival compared with IM or PM (Figure 03).

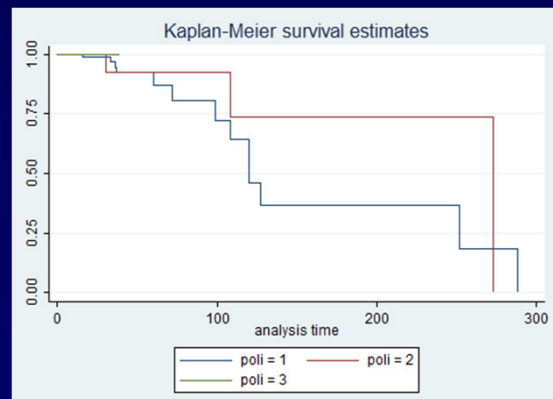


Figure 03:

poly1 = EM; poly2 = IM; poly3 = PM  
Vertical cumulative survival. Horizontally, time in months.

## DISCUSSION

The survival of patients EM, IM and PM was 59.2, 41.1 and 22.6 months, respectively, a difference that was not statistically significant. These data corroborate with Sirachainan et al. and Kumar et al, who observed that individuals with PM phenotype showed lower mean survival compared with patients with IM phenotype. On the other hand, Toyama et al. and Sukasem et al found no significant difference in disease-free survival between the different genotypes for CYP2D6. About recurrence, there was no significant difference between groups. This finding does not corroborate with Damodaram et al., who found a positive correlation between decreased function of the enzyme CYP2D6\*4 variant and recurrence of BC.

## REFERENCES

- 1 – HUBER-WECHSELBERGER, A. E. et al. Impact of CYP2D6 polymorphism on tamoxifen therapy: where are we? *Wien Med Wochenschr*, v. 162, n. 11-12, p. 252-61, Jun 2012.
- 2 – SIRACHAINAN, E. et al. CYP2D6 polymorphisms influence the efficacy of adjuvant tamoxifen in Thai breast cancer patients. *Pharmacogenomics Pers Med*, v. 5, p. 149-53, 2012.
- 3 – KUMAR, C. K. et al. Genotyping of tamoxifen metabolizing enzyme (CYP2D6\*4) and its clinical impact in breast cancer patients. *International Journal of Genetics and Molecular Biology*, v. 2, n. 1, p. 7, 2010.
- 4 – DAMODARAN, S. E. et al. Genetic polymorphisms of CYP2D6 increase the risk for recurrence of breast cancer in patients receiving tamoxifen as an adjuvant therapy. *Cancer Chemother Pharmacol*, v. 70, n. 1, p. 75-81, Jul 2012.
- 5 – SUKASEM, C. et al. Impact of CYP2D6 polymorphisms on tamoxifen responses of women with breast cancer: a microarray-based study in Thailand. *Asian Pac J Cancer Prev*, v. 13, n. 9, p. 4549-53, 2012