ROLE OF CYP19A1 GENE AMPLIFICATION AS A MECHANISM OF THERAPY RESISTANCE IN HORMONAL RESISTANCE METASTATIC BREAST CANCER PATIENTS

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Introduction

Breast cancer is the most frequent cancer among women. It is considered to be a highly heterogeneous disease, with distinctphenotypic and morphological profiles, causing very different clinical outcomes.

The CYP19A1 is used as a prognostic marker of breast cancer due to its genetic control in estrogen synthesis.

CYP19A1 is affected by prolonged use of aromatase inhibitors treatment, acquired resistance to hormonal therapy causes the tumor to relapse leading to metastatic breast cancers.

Aim of the work

The potential role of CYP19A1 gene copy number and amplification state was evaluated as a causative mechanism for developing secondary resistance to hormonal therapy in hormonal resistant breast cancer patients.

Patients and Methods

The study was conducted on 50 consecutively selected patients with recurrent and/or metastatic breast cancer presented to Clinical Oncology and Nuclear Medicine Department at Alexandria Main University Hospital.

Formalin fixed paraffin embedded tissue (FFPE) from primary tumor at the time of diagnosis and tissue tumor biopsies during relapse (confirmed by histo-pathological examination) from breast, liver, skin or any other affected organ if possible.

Tissue tumor DNA was extracted from FFPE.

The copy number of CYP19A1 gene was determined by Real Time Quantitative Polymerase Chain Reaction (RQ – PCR) using Taqman copy number assay (Applied biosystems).

Results

All the fifty patients (100%) had positive estrogen receptor tumors (inclusion criteria). Forty-four patients (88%) had positive progesterone receptors while none of patients had positive her2 receptors.

All patients enrolled in this study were subjected to endocrine therapy. Among them, twenty-five patients (50%) were on AIs (Femara and Aramidex) while twenty-one patients (42%) were on SERMs drugs (Tamoxifen and Nolvadex). About four patients (8%) were on combination of SERM and AI drugs (table 6).

The duration of endocrine therapy for patients ranged from 2-10 years with mean ± SD of 2.78 ± 1.30with median (IQR) 2.50 (2.0 – 3.0).no statical significant correlation between CYP19A1 gene amplification in the duration of endocrine therapy (p value=0.333).

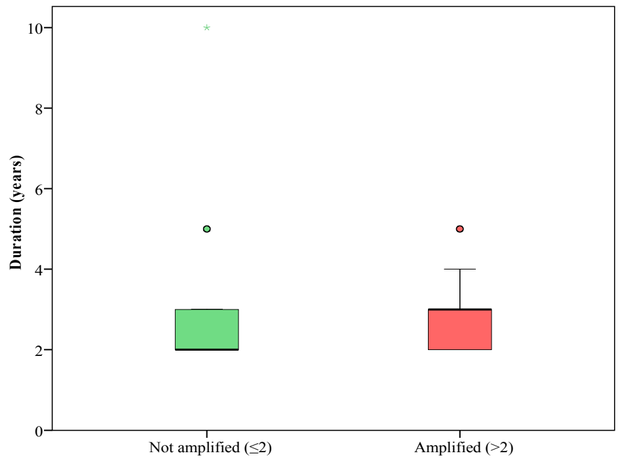

Figure 1: Relation between Copy number and duration (years)

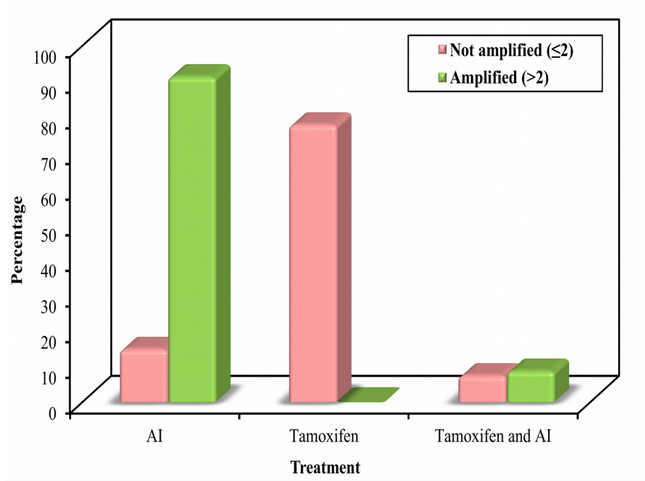

Figure 2: Relation between Copy number and treatment

Conclusion

In the current study it was found that CYP19A1 copy number amplification was increased in the secondary or recurrent tumor samples than in the primary. These results were not different to what has been reported in literature.