RS1008805 polymorphism in *CYP19A1* gene is related to the efficacy of hormone therapy in stage I–II and operable stage III breast cancer

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BACKGROUND: Aromatase, encoded by *CYP19A1* gene, catalyzes the final step of the conversion from androgens to estrogens. In premenopausal women, estrogen is mainly produced by the ovary, with a small amount being generated by aromatization of adrenal and ovarian androgen in extragonadal tissue.Whereas, in postmenopausal women, aromatization of androgen from extragonadal tissue becomes the prime origin of estrogen since the ovary ceases to function. Recently, it has been suggested that genetic polymorphisms in *CYP19A1* gene were related to aromatase activity as well as circulating steroid hormone levels in women. Population-based studies of *CYP19A1* gene polymorphisms have brought out controversial results with regard to their potential correlation with therapeutic efficacy of endocrine treatment.

HYPOTHESIS: It is biologically reasonable that *CYP19A1* gene polymorphisms may be associated with clinical outcome for hormone therapy in stage I–II and operable stage III breast cancer.

METHODS: Genotyping for *CYP19A1* rs1008805 polymorphisms was performed on 287 women with hormone receptor- (HR-) positive early breast cancer. Associations were evaluated between *CYP19A1* rs1008805 genotypes and disease-free survival (DFS).

RESULTS: Based on the analysis of the whole cohort, no significant differences were observed between rs1008805 genotypes and DFS. However, in postmenopausal women, rs1008805 variants were significantly associated with DFS (AA versus AG versus GG: 89.2 months versus 58.2 versus 32.7 months; P = 0.019). In addition, when the population was subgrouped into two cohorts, women carrying GG variant have a poorer DFS (GG versus AA or AG: 32.7 months versus 70.6 months; Hazard ratio (HR), 3.613; 95% CI, 1.380-9.457; P = 0.005). Furthermore, being adjusted by patients features in multivariate analyses, GG genotype remained an independent prognostic factor for DFS (HR, 3.439; 95% CI, 1.251-9.456; P = 0.017). However, there was no significant differences in DFS between women harboring the minor allele and those with the homozygous common allele (AG or GG versus AA: 52.4 months versus 89.2 months; HR, 1.288; 95% CI, 0.705-2.353; P = 0.408). Besides, there were no differences between rs1008805 polymorphisms and DFS among premenopausal women. The present study indicated that the homozygous minor allele (GG) of *CYP19A1* rs1008805 is significantly associated with worse clinical outcome of hormone therapy in postmenopausal HR-positive early breast cancer patients. If confirmed, genotyping for *CYP19A1* rs1008805 polymorphisms may provide predictive information for better selection of endocrine treatment.