BACKGROUND
HER2 (ERBB2, neu) is a proto-oncogene which encodes a transmembrane protein with tyrosine kinase activity. Trastuzumab (Herceptin®), a humanized monoclonal antibody which binds to the HER2 extracellular domain, is used for HER2 positive breast cancer’s treatment. Although it is well tolerated, it has a significant adverse effect: cardiotoxicity.

PURPOSE
To evaluate the possible effect of HER2 gene polymorphism at codon 655 (ATC/isoleucine to GTC/valine) (rs1136201) in cardiac dysfunction related to trastuzumab in women diagnosed with HER2 positive breast cancer.

RESULTS
Of all patients, 12 developed cardiotoxicity during the treatment with trastuzumab: 4 with genotype AA, 8 with AG and none with GG. (Table 2)

CONCLUSIONS
The results of our study show an association of ERBB2 polymorphism Ile655Val with cardiac toxicity associated with trastuzumab. Patients with genotype AG have higher risk of developing cardiac dysfunction related to trastuzumab than those ones with AA or GG. We need more studies on this polymorphism as well as larger sample sizes to confirm these findings.

MATERIALS AND METHODS
- 54 patients with HER2 positive breast cancer treated with Trastuzumab in our hospital were evaluated prospectively from January to December 2012. (Table 1)
- Trastuzumab was administered as a loading dose of 8 mg/kg followed by 6 mg/kg every three weeks.
- Cardiac function (left ventricular ejection fraction, LVEF) was checked at baseline and every 3 months by echocardiogram or MUGA (multigated blood-pool imaging) scan. We considered cardiac toxicity when LVEF drops 10 percentage points from baseline and below 50%, decrease of 15% respect to FEVI baseline or any decrease resulting in LVEF<45% at least one during the treatment or clinical manifestation.
- For genotyping we used TaqMan probes and allelic discrimination technique.
- Statistical analysis was performed with SPSS software packages and the level of significance was indicated by a p value lower than 0.05.

Significant correlation was not found between genotypes AA (vs AG+GG) or GG (vs AA+AG) and cardiac dysfunction. Instead, statistically significant differences were shown when comparing patients with genotype AA and AG+GG with cardiotoxicity (p = 0.039, OR= 4.0 95% CI= (1.03-15.60). If we adjusted the p-value according menopausal status at baseline this association was even stronger, (p=0.023, OR=5.12, CI= (1.17-22.45) (Table 3)

Table 1. Baseline characteristic of the patients included in the study

Table 2. Clinical characteristics of patients with cardiac toxicity and evolution during the treatment

Table 3. HER2 655 A/G genetic variant in cardiotoxicity and non-cardiotoxicity event adverse in HER2 breast cancer patients treated with trastuzumab.

*p-value adjusted by menopausal status