

## **The modification of response to treatment by non coding 3'UTR polymorphic variants in breast cancer patients**

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The analysis evaluates the relationship between the 3'UTR variants, clinical effects and response to chemotherapy. 33 germline polymorphisms were analyzed in 3'UTRs of ADME genes in 305 breast cancer patients treated with FAC (doxorubicin, 5'-fluorouracil, cyclophosphamide) regime. Measured clinical endpoints of this study were: overall survival (OS), progression-free survival (PFS), recurrence-free survival (RFS) and overall response defined as treatment failure-free survival (TFFS). The shortened OS was observed for the presence of *NR1/2* rs3732359 AA, *SLC22A16* rs7756222 CC, and *SLC22A16* rs9487402 allele G and clinical factors belonging to TNM classification: tumor size >1 cm, nodal involvement and presence of metastases. PFS pertained two polymorphisms *PGR* rs1824125 GG, *PGR* rs12224560 CC and *SLC22A16* rs7756222 CC and preexisting metastases. The shortening of RFS was observed for the *DPYD* rs291593 CC, *AKR1C3* rs3209896 AG and negative expression of PGR. The carrying of *ALDH5A1* rs1054899 allele A, lack of pre-chemotherapy surgery and negative status of PGR correlated with worse treatment response. We showed that common germline variants present in the population can be important factors determining the response to treatment. We also observed the role of the accumulation of genetic and clinical factors in poor survival prognosis and overall treatment response.