

3'UTR POLYMORPHISMS OF THE XMETS GENES AND ITS POTENTIAL EFFECTS ON THE FAC CHEMOTHERAPY IN BREAST CANCER PATIENTS.

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Xenobiotic metabolizing enzymes and transporters (XMETs) are involved in biotransformation, detoxification and transport of therapeutic drugs. Genetic variations in the XMETs genes may modulate an activity of anticancer drugs. Single nucleotide polymorphisms (SNPs) in the regulatory sequences of genes (3'UTR) may be the cause of the individual variation in treatment response in breast cancer patients and could lead to drug-resistance/drug sensitivity.

We examined the eleven 3'UTR SNPs in nine genes in 324 breast cancer patients treated with FAC first-line chemotherapy (FAC regime combines 5-fluorouracil, doxorubicin and cyclophosphamide). In this study we analyzed genes encoding proteins involved in FAC drugs transport (*ABCA1*, *ABCC4*, *ABCC1*), metabolism (*CYP1A2*, *CYP2E1*, *GSTM3*, *TYMS*) and drug-induced damage repair (*ERCC1*, *ERCC4*). Only functional polymorphisms in 3'UTRs of genes were selected for the analysis.

The impact of polymorphism on therapeutic toxicity was based on multivariate models based on 12 symptoms of toxicity. Preliminary results showed the effect of 3'UTR polymorphisms of the *ABCC1* and *ERCC1* genes on hematological therapeutic toxicity. The preliminary results of this study confirm the value of the previously developed by our team multifactorial model of therapeutic response predictions. The potential application of the results is seen in the choice of optimal treatment regimen for the patient and in improving the quality of life of patients during 5-fluorouracil, doxorubicin and cyclophosphamide breast cancer treatment.

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