Influence of *ABCB1* Polymorphisms on Therapeutic Response and Hematological Toxicity of Fisrt-Line Chemotherapy for Breast Cancer

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Introduction: ABCB1 is an efflux transporter, with physiological role on systemic distribution and disposition of many drugs, which may affect tumor sensitivity to chemotherapy. Polymorphisms in *ABCB1* gene reduce protein levels and enzyme activity, but their impact on the efficacy or toxicity of antineoplastics is not established. **Objective:** To investigate the influence of *ABCB1* polymorphisms (rs1128503 and rs1045642) on the hematological toxicity and therapeutic response of first-line breast cancer chemotherapy. **Material and Methods**: Women with first diagnosis of non-metastatic breast cancer, and treated with anthracycline and/or taxanes were included (N = 698). Hematological toxicity was based on blood cell count obtained from routine exams during chemotherapy cycles. Therapeutic response was evaluated by disease-free survival, and, after neoadjuvant chemotherapy, also by pathological examination of excised breast and lymph nodes. The association between polymorphisms and the outcomes of hematological toxicity or pathological response to neoadjuvant chemotherapy was evaluated by chi-square test, with calculation of odds ratios (OR). Polymorphisms were also evaluated for their impact on disease-free survival curves, with calculation of hazard ratios (HR), with COX regression for adjustment of significant covariates. **Results and Discussion**: Patients with rs1045642 TT genotype presented increased chance of moderate/severe neutropenia (OR = 1.61, 95%CI = 1.03-2.5; p = 0.028), whereas rs1128503 1236TT genotype increased the risk of breast cancer progression (HR = 2.1; CI =1.0-4,4; p = 0.048), despite its apparent benefit to complete pathological response of luminal tumors (OR = 2.7, 95%CI = 0.97-7.6; p = 0.05). **Conclusions:** The two studied *ABCB1* polymorphisms appear to have different effects on tumor or systemic cells: rs1045642 appears to increase the sensitivity of bone marrow or blood cells to anthracyclines and/or taxanes, possibly due to higher drug concentrations in the

blood, whereas rs1128503 compromised the disease-free survival, possibly due to lower drug concentrations within tumor cells.

Acknowledgements: CAPES, CNPq, FAPERJ, INCA and UNIRIO.**Key Words:** Polymorphisms, Breast Cancer, Chemotherapy.