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Core 5. Myocardium: Function and Failure

Session Title: Myocyte Survival and Regeneration in AMI and Heart Failure

Abstract 16961: Influence of Angiotensin Conversion Enzyme Gene Polymorphism on Cardiotoxicity Caused by Immunotherapy with Trastuzumab

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Introduction: Cardiotoxicity is the most important side effect of trastuzumab, humanized monoclonal antibody to the HER2 protein. Many molecular mechanisms and risk factors explaining cardiotoxicity have been identified, but it is still unclear how to assess individual risk. On the other hand, activity of ACE depends on ACE genotype and patients (pts) with D/D genotype have a higher cardiovascular risk.

Methods: In this study 130 pts with non–metastatic breast cancer were treated for one year, in adjuvant therapy, with trastuzumab. Pts were divided in two groups: 51 pts with proven cardiac toxicity during trastuzumab therapy were assorted to group A, and the control group B with 79 pts who didn’t have cardiac toxicity. Cardio toxicity was defined by echocardiography criteria. In both groups ACE gene polymorphism and plasma level of Nt-proBNP was determined.

Results: There was a significantly higher frequency of deletion mutant homozygous genotype (D/D) in group A in comparison with the control group B (49,02:22,78 %, p=0,0063). Mutant allele (D) was also more common in group A, but the difference is slightly above the significance (84,31:69,62 %, p=0,0575). Multivariate analysis revealed an increased risk of cardio toxicity in patients with the D/D genotype, a tumor of the left breast and with a positive family history of cardiovascular disease. A decreased risk of cardio toxicity was found in patients previously treated with FEC protocol (Picture 1). Complete recovery of the cardiac function had 54.9% of patients. There was no significant effect of ACE gene polymorphism on recovery of the cardiac function. The NT-proBNP level in the serum was significantly higher in the group that had evident cardio toxicity and especially with those who had irreversible cardiac attachment or only partial recovery.

Conclusion: Pts with D/D ACE genotype have a higher risk of developing cardiotoxicity with trastuzumab therapy and should be treated as high risk pts.

FEC chemotherapy - cyclophosphamide

Key Words: Immunologic factors - Gene mutations - Heart failure