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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

Ivo Darko Gabrić<sup>1</sup>; Hrvoje Pintarić<sup>1</sup>; Ljubica Vazdar<sup>2</sup>; Mario tefanović<sup>3</sup>; Marijana Jazvić<sup>4</sup>; eljko Soldić<sup>1</sup>; Rudolf Tomek<sup>5</sup>; Nada Vukelić<sup>3</sup>; Nada Vrkčić<sup>1</sup>; Danijel Planinc<sup>1</sup>

<sup>1</sup> Cardiology 2, UHC Sestre milosrdnice, Zagreb, Croatia

<sup>2</sup> Clinic for cancer, UHC Sestre milosrdnice, Zagreb, Croatia

<sup>3</sup> Clinical Chemistry, UHC Sestre milosrdnice, Zagreb, Croatia

<sup>4</sup> Oncology, UHC Sestre milosrdnice, Zagreb, Croatia

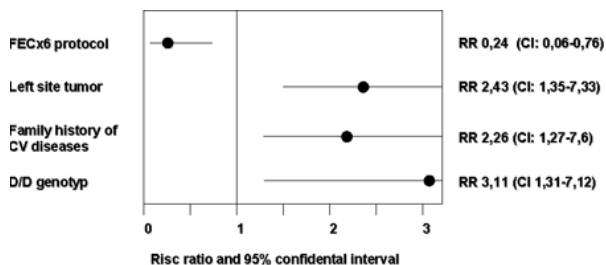
<sup>5</sup> Clinic for Cancer, UHC Sestre milosrdnice, Zagreb, Croatia

**Introduction:** Cardio toxicity is the most important side effect of trastuzumab, humanized monoclonal antibody to the HER2 protein. Many molecular mechanisms and risk factors explaining cardio toxicity 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 cardio toxic side effect during trastuzumab therapy were assorted to group A, and the control group B with 79 pts who didn't have cardio toxicity. Cardio toxicity was defined by echocardiography criteria. In both groups ACE gene polymorphism and plasma level of Nt-proBNP was determinate.

**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 cardio toxicity with trastuzumab therapy and should be treated as high risk pts.



FEC – fluorouracil+epirubicin+cyclophosphamide

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