655. Meta-Analysis of the Genome Wide Association Studies (GWAS) on the Intolerance of Angiotensin Converting Enzyme Inhibitors (ACEIs)

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Background: ACEIs are frequently used to treat hypertension and heart failure. Cough and angioedema are the two main adverse drug reactions (ADRs) associated with ACEI use that occur in up to 20% of the patients and are the main reason of therapy discontinuation.

Objectives: To identify single nucleotide polymorphisms (SNPs) associated with switching of an ACEI to an angiotensin receptor blocker (ARB) as a marker for ADRs.

Methods: A cohort of patients starting ACEIs was identified within the Rotterdam Study in the Netherlands and the GoDARTS study in Scotland. Cases were subjects that switched from an ACEI to an ARB while controls were subjects who used ACEIs for at least 2 years and did not switch. The validity of using switching as a marker for ACEI-induced adverse drug reaction (ADR) was investigated in a subset of users that had the primary care records available. A GWAS using an additive model was performed and results were meta-analyzed using METAL.

Results: In total 5109 ACEI starters were included in the study of which 959 were cases. The validation of switch as marker for ACEI-induced ADRs showed the positive predictive value of 90.5% for at least possible ADRs within a subset of 1132 patients. Ten SNPs within four genes reached the GWAS significance level in the meta-analysis. The strongest associated SNP was located on chromosome 17q25 (MAF=0.16, OR=1.52 [95%CI: 1.32-1.76], p=6.2x10-9).

Conclusions: These results indicate a substantial contribution of genetic variation in determining the risk of ACEI-induced ADRs, and warrant further studies in larger populations.

656. Long-Term Survival After Myocardial Infarction: Impact of Patient Non-Compliance to the EOLE Study Protocol

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Background: Non-compliance to secondary prevention is difficult to measure. Adherence to an observational study protocol may be a proxy for global non-compliance.

Objectives: To study the impact of patient non-compliance with study questionnaires on overall mortality.

Methods: EOLE is a cohort of post-MI patients followed yearly using patient questionnaires. Vital status at end of study was reconciled with the national death registry. Statistical analyses used Cox models with time-dependent variables.

Results: Of 5525 patients followed 6 years, 2715 provided data at all possible time-points during the study or before death (compliants (C)); for 2810 at least one time-point was missing (non-compliants, (NC)). At inclusion, C were older (63.0±12.3 vs 61.2±14.2 years), more often male (78.7 vs. 75.8%) and retired (58.9 vs 49.0%), with lower BMI (18.4 vs 19.3% above 30) than NC. Fewer C smoked (5.9 vs 12.6%), were diabetic (14.7 vs 18.9%) or had previous MI (12.1 vs 13.9%). There was no difference in hypercholesterolemia, excess triglycerides, hypertension, or in the inclusion MI. C were more often enrolled in a physical rehabilitation program (43.6 vs 38.8%); Post MI treatment was beta-blockers 90.7 vs. 88.5%, antiplatelet agents 99.6 vs.99.5%, statins 97.6 vs. 95.6% and ACEI/ARB 83.2 vs. 82.0%.

Overall mortality was 16.9‰ person-years (PY) in C vs 30.6 in NC. Coronary mortality in C was 3.9 vs