Reviewer's report

Title: Investigation of 95 variants identified in a genome-wide study for association with mortality after acute coronary syndrome

Version: 1 Date: 26 January 2011

Reviewer: Heribert Schunkert

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1) This study is rather underpowered as demonstrated by the power analysis provided by the authors. Only SNPs with very high Odds ratio and allele frequency approaching 50% will be detected with high probability. Therefore the significant association observed for rs 6922269 seems very much like a lucky finding.

2) I have concerns about the strong disparity between the discovery and the replication cohorts: The discovery cohort consists of Caucasians with a rather loose definition of ACS whereas the replication cohort consists mainly of African-Americans with ST elevation MI. Given the lack of power and the apparent differences in the two it is rather surprising that the authors were able to replicate SNP rs6922269 with marginal significance. This is either due to a very strong effect on mortality associated with this SNP that overrules differences in phenotypes and populations or, less attractive, constitutes a chance finding.

Please number your comments and divide them into

- Major Compulsory Revisions

1) We feel that the authors should provide replication in an additional cohort of ACS patients more similar to the discovery cohort. It would also be important to differentiate between all cause mortality and cardiovascular events in such a cohort. Such cohorts should be available through collaboration with other groups and the genotyping of just one SNP should not be too difficult to organize.