Reviewer’s report

Title: The Impact of Coronary Artery Disease Risk Loci on Ischemic Heart Failure Severity and Prognosis: Data from the COntrolled ROsvastatin multiNAtional trial in heart failure (CORONA)

Version: 1 Date: 4 August 2014

Reviewer: Markus Scholz

Reviewer’s report:

Major issues:
1. The CAD GWAS of Samani et al. (2007) used to select SNPs of interest in this study is outdated. Several new loci were found in recent meta-analyses comprising several more cases and controls (e.g. Schunkert, Nat. Gen. 2011). The authors should explain their choice, especially why they ignored more recent findings. On that note, GWAS references are outdated too.
2. I would strongly recommend re-arranging the results section and tables in a more reader-friendly way: At first, it is not sufficiently clear which models were analysed, i.e. what does “Cov 4” really means for the specific endpoints. I suggest specifying the clinical models (i.e. without genetics) first and then presenting the results of adjusted and non-adjusted genetic analyses. I also wonder why not all SNPs are reported in the tables. What are the SNP selection criteria for different endpoints? I recommend reporting all SNP results which could be helpful for subsequent meta-analyses.
3. Since this is a candidate analysis, more emphasize could be placed on analyzing different genetic models.
4. Since the majority of results are negative, I would suggest a power analysis to discuss the size of genetic effects detectable by this study.

Minor issues:
1. I think the applied Bonferroni correction does not make much sense. On one hand, much more than seven tests were calculated since multiple endpoints were analysed resulting in further accumulations of type I errors. On the other hand, I understand that this is a candidate study looking for alternative endpoints associated with CAD loci. Therefore, I would recommend dropping any Bonferroni corrections. Found associations should be discussed as suggestive requiring further replications.
2. Table 3: I have concerns regarding the Jonkeheere-Terpstra trend test for the endpoint “number of hospitalizations”. Since the endpoint suggests count data type, Poisson regression appears to be more appropriate. If the endpoint was divided into categories, this should be explained and justified in more detail.
3. Discussion: I think discussion of ANRIL was outdated too. There are more recent publications regarding this topic.
Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests