Reviewer's report

Title: Cytochrome P450 2C19*2 polymorphism in patients with stable coronary heart disease and risk for secondary cardiovascular disease events. Results of a long-term follow-up study in routine clinical care

Version: 1 Date: 16 October 2012

Reviewer: Willibald Hochholzer

Reviewer's report:

Overall an interesting analysis.

Major Compulsory Revisions

The major limitation is that it remains uncertain if the described association of CYP2C19*2 and clinical outcome is really a drug independent effect or caused in fact by subsequent clopidogrel treatment. To prove their thesis, the authors would need to provide separate analyses for patients on clopidogrel (either at enrollment or during follow-up) and patients that did never receive clopidogrel.

Minor Essential Revisions:
- Page 14, 1st paragraph: That the *2 polymorphism explains ~12% of the variability in response to clopidogrel might only be true in very homogenous populations (such as Amish people). In the European population, this impact appears to be smaller (J Am Coll Cardiol. 2010;55:2427).

Discretionary Revisions
- Page 14, 2st paragraph: These associations are only true if patients are also treated with clopidogrel! Therefore, analyses for the whole study population might not be appropriate.
- Page 9, second paragraph and Table 2: Can it be that the higher proportion of CYP2C19*2 carriers in younger subjects with lower education is due to differences in race (e.g., refugees from African or Asian countries? – in these countries, there is a higher prevalence of the *2 genotype).

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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

Declaration of competing interests: Received consultant fees from sanofi-aventis