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

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Reviewer: Betti Giusti

Reviewer's report:

This paper aimed to investigate the prognostic value for cardiovascular events at eight year follow-up of the status of carriers of the CYP2C19*2 polymorphism in a cohort of coronary heart disease (CHD) patients. The Authors studied and genotyped the CYP2C19*2 polymorphism in 1,050 patients with stable CHD.

Major Compulsory Revisions. I have the following concerns:

Abstract Background:
-“CYP2C19 polymorphisms are related to metabolizer phenotypes resulting in reduced effectiveness ……..” The sentence is not correct. In fact, the CYP2C19*17 polymorphism results in an increased effectiveness…..
- “An additional role of the genotype itself is discussed”, The Authors should clarify the meaning.

Abstract Methods:
-“Genotyping of one single……..follow-up. The Authors should improve the two sentences.

Abstract Results:
- The very few CYP2C19*2 homozygous patients are 27 subjects.

Abstract Conclusions:
- With respect to available literature data on this issue this cohort is a medium group not a large group of patients.

Introduction
- The introduction poorly addresses the needed background. Even if in brief, the Authors should better define the reference data on this topics.
- The Authors should clarify the meaning “The role of the genotype itself in patients with coronary heart disease (CHD) is not well described.”??

Methods
- Study population: - Clarify ….initial response 58%
- What is the statistical power of the study?
Results
- How many patients were on clopidogrel maintaining dose? The Authors should take in mind that the pharmacogenetic effect of the CYP2C19*2 polymorphism is possible whether the patients/subjects are on clopidogrel treatment.
- Table 2: Clopidogrel/ticlopidine: Is it possible that only 87 patients out of 1050 were on clopidogrel?
- The Authors should better describe the duration of the clopidogrel treatment.
- Did the Authors have information on the use of clopidogrel during the follow-up? This is a crucial information.
- The Authors should explain the rationale, the hypothesis, the aim to evaluate some parameters measured (e.g. NT-proBNP, Cystatin C, IL-6, etc) according to CYP2C19*2 genotype.

Discussion
- The very few CYP2C19*2 homozygous patients are 27 subjects.
- How do the Authors explain the risk of homozygous carriers without clopidogrel? Also in consideration of the large trials results evaluating the effect of the CYP2C19*2 polymorphism in patients on antiaggregant therapy different from clopidogrel.

- The paper is poorly written and suffer from poor organization.

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

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests