Reviewer's report

Title: Prognosis of concomitant users of clopidogrel and proton-pump inhibitors in a high-risk population for upper gastrointestinal bleeding

Version: 1 Date: 7 October 2013

Reviewer: Kathryn Momary

Reviewer's report:

Thank you for providing me with the opportunity to review this manuscript assessing CVD risk in patients receiving concomitant PPIs and clopidogrel. The authors explore this question in a unique patient population.

Major concerns:

• The authors do not differentiate between those PPIs most likely to effect clopidogrel and those less likely. This needs to be at least discussed or mentioned in the background and methods.

• The inclusion criteria as it relates to CVD are quite wide. Specifically the inclusion criteria are AMI, stroke and angina. In the US, clopidogrel is not routinely used for stroke or angina. Please justify the inclusion of these disease states into your study.

• Since the majority of CVD patients will receive both aspirin and clopidogrel, their exclusion makes this data difficult to interpret. This definitely limits the clinical applicability of this manuscript and this needs to be addressed by the authors.

• The different PPIs used needs to be described in table 1.

• The authors do multiple sub-group analyses (time of bleed and different types of CVD). This is complicated and the text in the results does not clearly outline the different groups. Perhaps breaking the results up into section by subgroup analysis would make this clearer.

• The authors only cite and discuss literature that supports an interaction between PPIs and clopidogrel. However, there is a significant amount of literature where no interaction was seen. The 3rd paragraph of the discussion section needs to more clearly describe the totality of literature related to this topic.

Minor comments:

• Abstract: Please explain what CVD encompasses in the abstract.

• Please provide a reference for the co-morbidity scoring system used.

• The authors state in the last paragraph of the methods section that patients who had a GI bleed after the study period are at increased risk of bleed during the study period. This needs a reference to support the statement.
• The second sentence in the results section does not make any sense. Please revise.
• While table 2 shows both the CVD cohort and the AMI cohort, this is never clear in the text and the different results aren’t discussed.
• The last sentence of paragraph 2 in the discussion section does not make sense.

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

**Quality of written English:** Not suitable for publication unless extensively edited

**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.