Reviewer’s report

Title: Safety and efficacy of long-term esomeprazole 20 mg in Japanese patients with a history of peptic ulcer receiving daily non-steroidal anti-inflammatory drugs

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Reviewer: Morten Würtz

Reviewer’s report:

Sugano and colleagues submit a manuscript considering the efficacy and safety of once-daily omeprazole in patients with prior GI ulcer concomitantly treated with NASIDS. An open-label design is used, and 130 patients are included and followed for 12 months. The authors conclude that omeprazole 20 mg once daily is well tolerated and effective in preventing adverse events (including recurrent ulcer).

I congratulate the authors with a well-designed and meticulously conducted study. The manuscript is well written. The following issues must be addressed:

Major compulsory revisions:

1. About one quarter of the patients received concomitant corticosteroid treatment. Corticosteroids likely increase the risk of abdominal complications due to a reduced ulcer healing and increased bleeding tendency. This deserves a mention. Despite the fact that the study seems underpowered for subgroup analyses, the authors may want to include “+/- corticosteroid treatment” in Table 4.

2. Compliance is measured by pill counting and NSAID diaries. These are not very strong compliance parameters, although I acknowledge that they are the only feasible options in the current study. I think the compliance issue deserves a mention under Limitations.

3. I do not find any information on the duration of NSAID treatment prior to study start. The risk of NSAID-induced GI complications (including ulcer) must depend on how long NSAID treatment has been ongoing. A patient that starts taking NSAID very shortly prior to being included in the study has another a-priori risk of GI complications than a patient who has been treated with NSAIDs for years. Would the authors please try to address this issue?

4. I appreciate the inclusion of CYP2C19 genotyping. However, there are no details on what specific SNPs the authors looked for. Was it the *2 polymorphism? Please elaborate a little in the Methods section.

5. Regarding Figure 1: The figure would benefit from a little more details: some words to describe the main reasons for ineligibility in the 247 patients being excluded. This is important, because some extent of selection bias is likely to be found here.
6. Regarding Table 3: The authors report the most frequent adverse events. I have a problem with the mix of subjective symptoms (e.g. headache and pruritus), objective signs (e.g. hypertension and eczema) and biochemical measurements (e.g. GGT levels and platelet count) under the heading “Adverse events”. For instance, in my view elevated GGT levels are not an adverse event per se, but they reflect liver damage caused by whatever reason. Such damage may be due to true adverse events like infectious hepatitis, toxic hepatitis, and autoimmune hepatic disease and so on. I suggest dividing the content of Table 3 by use of subheadings to distinguish between symptoms, objective signs and biochemistry.

Minor essential revisions:

1. The reference list should be extended to include up to 30 authors before using “et al”.
2. The use of LANZA scoring (and the frequent endoscopies) is an obvious strength. Although the LANZA score is well-known, for the sake of the readers of the journal you may want to expand your description of this scoring system in Methods. A single sentence describing the content of the LANZA score would be helpful to many readers.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**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