Reviewer's report

Title: Possible etiology of improvements in both quality of life and overlapping gastroesophageal reflux disease by proton pump inhibitor treatment in a prospective randomized controlled trial

Version: 1 Date: 16 July 2013

Reviewer: Yeong Yeh Lee

Reviewer's report:

The current clinical trial indicates that the PPI, pantoprazole 40 mg daily is effective in relieving symptoms and sustaining improvement in quality of life for at least 6 mo in patients with GERD overlapping with functional upper and lower GI symptoms. This study addresses a rather common scenario of patients that GI clinicians often encounter.

Major compulsory revisions

1. A section in methods should be created for data and statistical analysis. Descriptions of analysis and statistics mentioned in the assessment of GI symptoms and HRQOL are to be moved into this section. Please clarify whether the ReQuest™ scores in the results were reported in mean or median (mean mentioned in Figure 2).

2. Results; are there any differences in symptoms and HRQoL improvement between different grades of esophagitis?

3. Discussion; the authors proposed the sustained improvement of functional symptoms with PPI over time could be immune-mediated but evidence were lacking and remain largely speculative. Likewise, current data on genetic polymorphisms being useful in such circumstances is also speculative and should be tone down in the conclusion in the abstract. The improvement seen is likely to be multifactorial.

4. Discussion; limitations of study were not mentioned. One would be a small number of patients in subgroups of FD and IBS. This study did not address patients with the more prevalent endoscopy-negative GERD, who are more resistant to PPI. Lack of a control group with purely functional symptoms

Minor Essential Revisions

1. Page 6, Methods, study design and patients, line 3 – need to rephrase the sentence “In brief, this randomized, multicenter……” and clarify treatment intensity comparison and diagnosis of GERD which was based on the presence of erosive esophagitis (LA classification) and symptoms.

2. Page 6, Methods, study design and patients, line 7 – is it treatment “endpoints” or “concepts”?

3. Page 7, Methods, study design and patients, line 18 – functional missing from
“dyspepsia”, FD was used in quoted reference 16. Also maintain consistency of use for the term FD throughout the manuscript.

4. Page 9, Results, therapy-associated change in GI symptoms, para 2, last sentence – there is no need to mention “highly” and it is appropriate to report p value for each comparison.

5. Page 12, Discussion, para 1, line 10 – remove “e” from the sentence.

**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.