Reviewer’s report

Title: Symptom profile in partial responders to a proton pump inhibitor compared with treatment-naïve patients with gastroesophageal reflux disease: a post hoc analysis of two study populations

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Reviewer: Edoardo Savarino

Summary and Comments

The article entitled “Symptom profile in partial responders to a proton pump inhibitor compared with treatment-naïve patients with gastroesophageal reflux disease: a post hoc analysis of two study populations” by Vakil et al. is a post-hoc analysis whether differences in terms of symptom profiles exist in partial PPI responders vs. treatment-naïve patients with gastroesophageal reflux disease (GERD).

The main results of the investigation is that gastrointestinal symptom patterns in partial PPI responders were similar to those in treatment-naïve GERD patients, but partial PPI responders experienced more severe reflux symptoms (heartburn and regurgitation) on PPI therapy than did patients with GERD not treated with PPIs. Thus, the authors concluded that the main symptom burden of patients with GERD who are partial responders to a PPI continues to be heartburn and regurgitation.

Current study is clear and well written. Also the main idea of the study is interesting and the conclusion appear somehow surprising since recent data (Gut. 2012 Apr;61(4):501-6, Gut. 2009 Sep;58(9):1185-91) underlined that concomitant functional gastrointestinal disorders play a major role in favouring PPI partial response or refractoriness, more than the persisting presence of heartburn and regurgitation. Thus, it is really interesting from my clinical point of view.

Minor Compulsory Revisions:

1. Methods. A major limitation of the PRO validation study is that symptoms relief has been evaluated after a short PPI trial (4 weeks). Indeed, 12 weeks represents, to date, the best time interval before defining patients as responders or non-responders to PPI therapy (Gut 2012, 61(9):1340–322 1354). Moreover, it is not clear if PPI was given at single or double dose. Also in the Diamond study the duration of PPI trial was too short and at low dosing. Please, clarify and discuss.

2. Discussion. Given the final conclusion on the relevance of heartburn and regurgitation in favouring partial PPI response, the role of weakly acidic or bile reflux should be more emphasized in the discussion section.
3. Discussion. I would eliminate the term “well-defined” patients population since the criteria used to define GERD are different in the two studies as well as the criteria used to define patients as partial responders (see above)

4. References. There are few important and more recent articles about the overlap between GERD and functional GI disorders that have not been cited (J Gastroenterol. 2014 Apr;49(4):628-37 ; Gut. 2009 Sep;58(9):1185-91; Nat Rev Gastroenterol Hepatol. 2013 Mar;10(3):175-86; World J Gastroenterol. 2013 Sep 21;19(35):5787-97)

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

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'