Author's response to reviews

Title: Impact of 5-HT3 receptor antagonists on chemotherapy-induced nausea and vomiting: a retrospective cohort study

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Author's response to reviews: see over
Dear Editor,

Many thanks to you and your reviewers for your thorough review and feedback. Please note that we have revised the manuscript to reflect the accommodation of most of the reviewers’ comments. Below please find specific changes to each one of the reviewers comments. All changes have been indicated with tracking marks in the manuscript. Please let me know if you have any questions.

Sincerely,

Hind T. Hautom

Reviewer 1

Although, the data presented are interesting because of the huge number of the patients observed, the paper is too long and should be adapted to a short communication.

Response:
We respectfully believe that short communication will not be adequate to inform the readers about the study design and outcomes. Moreover, we are guided by the lack of similar request from the other reviewers. We have, however, slightly shortened the manuscript by condensing some of the sentences.

Reviewer 2

<Major Comments>
1) Title “Impact of step therapy…” should be changed, because this research is nothing to do with step therapy. Even if there might be some cases related with step therapy, this research is not designed to evaluate the step therapy.

Response:
We have removed ‘step therapy’ from the title.

2) The database, insurance type plan, health maintenance organization and American Managed Care Pharmacy commissioned report utilized here in this research should be introduced precisely, as all the reviewers and readers of this manuscript are not US citizens. Especially the system of PharMetrics’ claims database is profoundly related to the quality of this research itself.

Response:
Detailed information on AMCP and PharMetrics has been added to the manuscript.
3) The Impact of NK1ra and dexamethasone should not be ignored, when you compared palonosetron and other 5HT3ra, which was not considered in this investigation.

Response:
All NK1RA and dexamethasone prescriptions were included in this study. As stated in the manuscript “When the utilization of aprepitant and dexamethasone were included, the total number of antiemetic claims in the palonosetron groups remained significantly lower than the total claims for the older 5-HT3 RA groups among all three cancer cohort (all p<0.0001).”

4) There must be discrepancies between prescription by physicians and actual intake by patients. Does the database utilized here reflect prescription rather than intake? If physicians tend not to prescribe additional antiemetics for palonosetron group, as they believe it’s efficacy, the bias is induced easily.

Response:
PharMetrics contains paid claims data, which indicates a prescription has been filled, paid, and received by a patient. Although a 100% intake or compliance with the medication taking cannot be guaranteed, judging from the severity of the condition, it is likely that patients who filled the prescriptions had also taken the medications.

<Minor Comments>
1)”CCI” should be explained in Abstract.

Response:
Done.

2)Which is more reasonable "More CT days reduced the number of CINV days” described in RESULTS or “long CINV days might be the cause of less CT days”?

Response:
To address the concern, we have changed the statements to reflect that CT days were associated with fewer CINV days.

3) The reviewer respects the authors about the unique approach using claims database and the results shown in this manuscript must reflect some real outcome of our medical services though, each problem described above needs to be solved or considered.

Response:
We have addressed the aforementioned issues.

Reviewer 3
Formatting comments:
• Abstract – results section. Meaning of the CCI acronym is not specified

Response:
Done.

• Background section. At the end of the sentence “The available pre-clinical and clinical evidence suggests that control of CINV in the delayed phase is a true pharmacological effect ….” A reference should be entered, may be Rojas articles about 5-HT3RA interaction with serotonin receptor.

Response:
Reference added.

• Table 1. Acronyms should be specified and for Age authors missed to indicate if it is in mean or median and range of age could be an useful data.

Response:
Acronyms have been specified, and age information was presented as mean and standard deviation as conventions.