Author’s response to reviews

Title: Pathogenetic approach to the treatment of functional disorders of the gastrointestinal tract and their intersection: Results of the Russian Observation Retrospective Program COMFORT

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Author’s response to reviews:

Dear Dr. Bellini,

First of all let me thank you and Dr. Facciorusso and Dr. Stasi for a tremendous job and valuable comments.

We revised the manuscript and made all required changes highlighted yellow and we believe it will help us to improve our manuscript to be published in BMC Gastroenterology.

We agreed with all reviewers’ comments, made all the necessary corrections in the text. Please find the corrected version in the attachment.

Due to the report of Cristina Stasi:

1) We specified the study period in the Abstract (please find page 1, lines 6-7)

“The subjects of the observational noninterventional retrospective program were the data of 14,362 outpatient records of patients with diagnosed FD, IBS, and/or overlap, who were observed by gastroenterologists from November 01, 2017, through March 30, 2018, who received the drug Kolofort in monotherapy for 12 weeks, 2 tablets twice a day.”
2) We admitted the better structure would be if we move the text about the previous studies from Background to Discussion. You will find this abstract highlighted yellow (page 10 (the last line) and page 11).

3) We pointed out information about the cites

In accordance with the type of the study we took into consideration the number of gastroenterologists. So, in order to obtain a representative sample, data of 14,362 patients from 67 cities of Russian Federation were taken. 473 gastroenterologists participated in this study.(page 4, line s 3-5)

4) We clarified the diagnostic criteria for FD and IBS (Methods, page 4, lines 10-22).

Patients were evaluated according to the recommendations of the Russian Gastroenterological Association for the treatment of FD and IBS.

FD is characterized by the presence of permanent or periodic symptoms of dyspepsia, such as upper abdominal pain, nausea, a feeling of burning in the stomach area, fullness in the stomach, early satiety, which appeared at least six months before diagnosis, lasting at least 3 months, in the absence of an organic disease that explains the appearance of these symptoms.

Based on the Rome IV Criteria IBS is manifested by a symptom-based scheme requiring that patient complains of abdominal pain on average at least once per week and that pain is associated with two or more of the following characteristics: it is related to defecation; it is associated with a change in the frequency of stool; or it is associated with a change in the form of the stool. These criteria should be fulfilled for the last 3 months, with the onset at least 6 months before diagnosis.”

5) We reported the eligibility criteria (page 4, lines 7-12, page 5, lines 5-9).

“The study included the analysis of medical records of outpatients 18 and older, of both genders, diagnosed with FD or IBS or with a combination of FD and IBS, as verified by their medical history. To be included in the study, patients had to be observed by a gastroenterologist from November 01, 2017, through March 30, 2018. Patients were evaluated according to the recommendations of the Russian Gastroenterological Association for treatment of FD and IBS.
All study participants signed the informed consent form. The observational type of the study did not imply additional methods of laboratory or instrumental examination for the inclusion of patient's data in the program. Patients with decompensated or unstable somatic disease, patients showing alarm symptoms, patients with significant accompanying gastrointestinal or other diseases, pregnant or nursing women were not admitted to the study.

6) We made a detailed description, illustrating the selection of 9,254 of the 14,362 total. (Page 12, line 20-till page 13, highlighted yellow)

Inability to include the data of 5,108 patients can be also considered as a limitation of the current study. At the same time, we should emphasize that some doctors might have experienced some difficulties with the filling of the various forms, thus the information on 3463 patients was missing.

As previously mentioned, the data of 1645 patients with concomitant organic diseases of the GIT were not taken into account in the analysis of efficiency, since the overlap of these diagnoses can occur in case of their incorrect differential diagnosis.

Furthermore, in accordance to Rome IV criteria these cases might be considered as secondary dyspepsia, which goes against the inclusion criteria.

7) To structure the manuscript we added the Limitations section and pointed out the main ideas that might be considered as limits. (please find pages 12-13 “Limitations”)

We also took into account all the comments of Antonio Facciorusso

1) We admit that the questionnaire 7*7 is not validated in countries other than Russia, as well as the retrospective nature of the study is influenced by the patient's subjective perception of the symptoms and we mentioned it in the Limitations section. (Page 13, lines 1-3)

2) We made a detailed description, illustrating the selection of 9,254 of the 14,362 total. The similar comment was made by Dr. Stasi and is pointed out above.

In accordance with the “7*7” questionnaire absolute and relative indicators (%) are used for the qualitative study data, and medians and quartiles for the quantitative data. A decrease in the number of points according to the questionnaire “7*7” by 50% or more can be considered as a significant response to the treatment.

4-5) We improved English grammar (the whole text and mentioned Dr. Kovalchuk in the Acknowledgments) and clarified the statistical analysis in the Materials and Methods section.

Dear Dr. Bellini,

May we clarify the formal writing ability of the authors’ names? We’ve noticed that in Research Square system some of our authors had the 1-st letter of the patronymic name (e.g., Mikhail A Putilovskiy) and other authors don’t. Though all authors are mentioned with name, surname and 1 letter of the patronymic name on the title page.

Kind regards,

Dr. Glazunov