

## ANSWERS TO REVIEWERS



September 7, 2016

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 28868-editorial.doc).

**Title:** Possible therapeutic role of IgE blockade in irritable bowel syndrome

**Author:** Eli Magen, Tinatin Chikovani.

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 28868

The manuscript has been improved according to the suggestions of reviewers:

1 Format of abstract and core tip have been updated

2 References and typesetting were corrected.

3 Revisions have been made according to the reviewers' suggestions:

### **Response to Reviewers' Comments**

Reviewer ID 02531171:

Response:

**We thank the reviewer for her/his valuable comments which helped to considerably improve the quality of the manuscript.**

Abstract: as suggested, we have described what omalizumab is and its mechanism of action on first mention in the abstract and also have indicate what is being discussed in the editorial.

Core tip: as suggested, the format of core tip has been updated.

Introduction: as suggested, we introduced some context about the influence of early-life stress on inflammatory response in patients with IBS.

As suggested, the importance of mast cells has been introduced before suggesting a treatment that would target that specific aspect of IBS pathophysiology.

We have named each abbreviation on first mention (both in the abstract and the main text).

Main body of editorial:

'Enteric motility' (pg 5) would probably be accurately describes as gut motility regulated by the enteric nervous system.

The second paragraph 'Both histological samplings....' would be a better opening paragraph to this section, to provide an understanding of immune activation in this disorder, which is only just being accepted as part of the etiology of the disorder.

Answer: As suggested, the place of the second paragraph 'Both histological samplings' has been changed to be the opening paragraph to this section.

More detail on the encouraging clinical results of MC stabilisers is needed.

Answer: As suggested, the relevant information and references have been added to the section.

Some discussion of low FODMAP diets would be interesting in the section entitled 'IBS and food hypersensitivity'. This is a controversial area with several meta analyses of clinical interventions unable to detect beneficial effects of food elimination.

Answer:

As suggested, this discussion has been added to the section.

Is urticaria or asthma common in IBS or was the effectiveness of anti IgE treatment in these patients a felicitous finding.

Answer:

The new section "Prevalence of asthma and urticaria in patients with IBS" has been added to discuss about prevalence of these disorders in patients with IBS.

More details on the experimental strength of the two key experiments are needed (ie. numbers of patients etc) The title 'Anti IgE therapy can abolish to downregulate mast cell activity in IBS' does not make sense.

Answer:

The suggested discussion has been added to the section "Clinical evidence of anti IgE therapy efficacy in IBS". The title 'Anti IgE therapy can abolish to downregulate mast cell activity in IBS' has been changed.

This section needs some concluding remarks about how the changes in mast cells could underlie symptom improvement.

Answer:

As suggested, some concluding remarks about how the changes in mast cells could underlie symptom

improvement have been added.

The Conclusion section needs a good deal of work – it should not simply be a reiteration of some of the work discussed in the editorial. Do the authors believe they have found the cure for IBS? How will the field change following the two clinical studies demonstrating favourable effects of this new treatment strategy. Will this be effective in all subtypes of IBS?

Answer:

As suggested, the conclusion section has been rewritten and now includes our view of anti IgE therapy in the management of IBS.

Reviewer ID 03474957

Response:

**We thank the reviewer for her/his valuable comments which helped to considerably improve the quality of the manuscript.**

The role of IgE in IBS is worth further consideration however; these medications are incredibly costly as they are in their infancy. This needs to be mentioned in the conclusion and I do not believe that it will be a feasible treatment option in all patients with IBS. These medications have the potential to work in a subset of IBS patients although as of yet we do not understand the underlying pathophysiology. Those with atopy (and elevated serum IgE levels) may derive the most benefit from these medications.

Answer:

We completely agree with the reviewer and as suggested these remarks have been added to the manuscript.