Author's response to reviews

Title: Improving lactose digestion and symptoms of lactose intolerance with a novel galacto-oligosaccharide (RP-G28): a randomized, double-blind clinical trial

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Author's response to reviews: see over
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Dr. Nagaraj Nagathihalli
The Nutrition Journal Editorial Team

We would like to thank the editorial team, Dr. Eamonn Quigley, and Dr. Vincenzo Savarino for taking the time to review our manuscript entitled “Improving lactose digestion and symptoms of lactose intolerance with a novel galacto-oligosaccharide (RP-G28): a randomized, double-blind clinical trial”. We have thoroughly evaluated the comments provided by both reviewers, and believe that our revisions have accurately addressed their concerns. A detailed overview of our revisions can be found below:

Q1: What was/were the primary endpoint/s? This is critical; the authors performed a power calculation which means that they must have defined at least one primary endpoint but I cannot make out what that was.

Primary endpoints were added to the body of the manuscript on page 6. Additionally, we added Table 2, which lists all primary and secondary endpoints.

Q2: Efficacy was calculated on the PP, not the ITT population; this is far from an ideal approach. At the very least, both the PP and ITT data should be presented.

We added a response to this comment at the bottom of page seven in the manuscript and the first paragraph under “RESULTS” on page eight. The ITT population includes patients who did not submit data on Day 36 so an efficacy analysis could not be completed. The PP population includes every patient that completed Day 36.

Q3: What were the prescribed (rather than post hoc) secondary endpoints? This must be clarified.

Please see the response to question 1.

Q4: What was the precise schedule of dose escalation; was this also performed for the placebo?

We added language on page five to clarify that the dose escalation was performed for both RP-G28 and Placebo. We also referenced a dose escalation table on the top of page six and added Table 1, which shows the dose escalation.

Q5: Subjects were excluded due to product discoloration; why were placebo subjects also excluded for this reason?

Added language in the bottom paragraph of page eight that explains why placebo subjects were also excluded. The study was double blinded and both placebo and RP-G28 subjects had to be removed in order to not break the blind.
Q6. I cannot understand the presentation of the HBT results. The tables present data on deltas and the authors could, I assume, present AUCs but instead refer to a "random likelihood" calculation which was never mentioned previously and is not explained in any detail. Also, the abstract refers to trending of data but the results suggest that differences were significant.

The HBT results section on page nine was edited to make the presentation of the HBT results more clear. A p-value was added to the caption of Table 3 which presents the HBT results. The random likelihood calculation was further clarified as simply an observation and not part of the primary / secondary endpoint analysis. Additionally, a p-value was added to the caption of Figure 3, which correlates to the “trending of data” mentioned in the manuscript.

Q7: Did the Authors exclude patients with celiac disease from the population they studied?

Language was added on page five that explains that patients with celiac disease were excluded from the studied population.

We look forward to hearing your response.

Sincerely

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